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JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY AUGUST 22 1953

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 22 1953

THE HUNTERIAN ERA: ITS INFLUENCE ON THE ART AND SCIENCE OF SURGERY*

BY

LIONEL E. C. NORBURY, O.B.E., M.B., B.S., F.R.C.S.

Consulting Surgeon, Royal Free Hospital, St. Mark's Hospital, and Belgrave Hospital for Children

In 1813 Dr. Matthew Baillie, a nephew of John Hunter, a distinguished physician and pioneer in the study of morbid anatomy, and Sir Everard Home (Hunter's brother-in-law), comparative anatomist and surgeon, executors, being desirous of showing a lasting mark of respect to the memory of the late John Hunter, inaugurated an oration to be called the Hunterian Oration, to be delivered in the theatre of the College on February 14, the birthday of John Hunter, or as near that date as possible, by the Master or one of the Governors for the time being, or a member of the Court of Assistants; such oration to be expressive of the merits in comparative anatomy, physiology, and surgery, not only of John Hunter but also of all such persons as should be from time to time deceased, whose labours have contributed to the improvement or extension of surgical science.

It will be agreed that the terms of reference, as enunciated by the founders of the Hunterian Oration, are wide, and the scope available to the orator considerable. Yet a study of John Hunter's writings and those of his contemporaries makes one realize the universality of this great man and his teaching—how much has been left unsaid and what inferences still remain to be drawn from his scientific researches. This is especially brought home to one after a study of various Hunterian Orations from the time of their inception in 1814, when the oration was delivered by Sir Everard Home, up to the present. The orator is thus enabled to glean inspiration from the researches of those who have previously held this post of honour. One is, however, left with a sense of frustration as to what unexplored fields of activity remain, and what further influence on the science and art of surgery can be brought to light, having its roots in the life and work of the great master, John Hunter.

John Hunter's Early Training and Character

It is a debatable point whether John Hunter was born on February 13 or 14, 1728. We in this College commemorate his birthday on the 14th.

Stephen Paget records that as a boy John Hunter was deficient in self-control—idle and ignorant; but he showed great neatness of hands and quickness of perception in anything mechanical, though he remained obstinately impenetrable to book-learning. The cultivation of the powers of observation was a great asset to Hunter. The seed was undoubtedly implanted in his mind during early childhood when he lived in the family house of Long Calderwood, in Lanarkshire, with its farm and beautiful countryside. Instead of attending school he would play truant and spend time in the country imbibing the knowledge that Nature had to teach. To quote from an article on "Long Calderwood," written by Sir Arthur Porritt and published in the *Annals* of the College: "The interest of Long Calderwood to us of the Royal College of Surgeons of England lies in the fact that it provided the background for the first sixteen or seventeen years of John Hunter's life, and must have had a great formative effect on the future development of the genius of our patron saint." It is indeed good news to hear that, under the auspices of a Scottish Corporation, the property of Long Calderwood has been acquired for the purpose of its protection and maintenance as a "National Memorial."

Hunter the Man

As a man, John Hunter has been described as short, red-haired, pugnacious, but very kind; a natural philosopher seeking a clue to human ills by studying the comparative anatomy of animals, birds, and fishes. He was easily provoked and hated deceit. He was a craftsman of no mean order, having in his early days worked in a carpenter's shop under the direction of his sister's husband, Mr. Buchanan.

His work came first, much to the detriment of his wife and family, both socially and financially. Dr. Joseph Adams, in his *Life of John Hunter*, published in 1817, says: "John Hunter's countenance was open, and, though strongly impressed with thought, was by no means habitually severe, but softened into tenderness or sparkled with brilliancy, according to the impression on his mind."

Rudolf, in his address on "Hunteriana" delivered before the Hunterian Society in April, 1951, when referring to the character of John Hunter, said: "At home he was a model husband adored by his pupils and intimates, but to the outside world, a changed being, quarrelsome and disputatious."

His home in Leicester Square, where he spent his last days, was, it is supposed, the *mise en scène* for Robert Louis Stevenson's story *Dr. Jekyll and Mr. Hyde.* A suggestion of this dual personality is discernible in Hunter's character. Paget states that John Hunter was "emotional and impetuous—quickly moved to tears of sympathy, quickly ablaze with anger and fierce word."

One may compare the temporary anger of Hunter on occasions with his friend and pupil Edward Jenner,

*Shortened version of the Hunterian Oration delivered at the Royal College of Surgeons of England on February 13, 1953.

which was soon followed by a letter of apology and a reconciliation, or, again, "Hunter's violent anger just before he died at St. George's Hospital."

In spite of his temperamental nature, Hunter retained an abundant sense of humour, as instanced by some of the letters to his brother William. The following are abstracts of a few of these. One, written before 1780 :

> Dear brother,
> The bearer is very desirous of having your opinion. I do not know his case. He has no money, and you don't want any, so that you are well met.
> Ever yours,
> John Hunter.

In a letter written to William dated September 28, 1761, when on active service, he says : "My fellow creatures of the hospital are a damn'd disagreeable set." In another, dated May 28, 1762, when on active service, he says: "I am obliged to be physician and everything else, and I think I do as well as the best of them." Another letter to Jenner dated January 29, 1789, in reply to one from Jenner asking Hunter to be a godfather to his child : "I wish you joy—it never rains but it pours. Sooner than the brat should not be a Christian, I will stand as godfather, for I should be unhappy if the poor little thing should go to the devil because I would not stand as godfather. I hope that Mrs. Jenner is well and that you begin to look grave now you are a father."

FIG. 1.—Sir Everard Home.

The Royal College of Surgeons is fortunate in possessing many of John Hunter's original letters. They are written in a clear and legible hand, so different from the handwriting of the majority of medical men of the present era.

In studying the character of John Hunter, one is struck with the comprehensiveness of the man. With him, medicine was the same as all science connected with life. One discovers an earnestness, and a grasp of understanding of natural objects which is phenomenal. He had no time for any study of men's devices. With all his roughness of manner, John Hunter carried an honest independence. He never truckled for advancement nor sought favours, but was at all times more ready to give than to receive.

He had to wait a long time before practice came to him, but in due course his income reached a figure of six thousand guineas a year. A goodly income, but one which in his case went to the advancement of science —to the development of medicine and to the foundation of the incomparable treasures which now are in the possession of the College.

It is recorded that when Hunter's portrait was placed before Lavater, the physiognomist, after deep study he exclaimed : "That man thinks for himself."

Cline, in a Hunterian Oration, says : "Much as Hunter *did*, he thought still more. He often told Mrs. Cline that his delight was to think."

Abernethy, in his Hunterian Oration of 1819, says that Hunter was "profoundly contemplative, his mind had not been taught to act in imitation of others ; he disliked to read as much as he liked to think."

Travers wrote : "He was capable of large and comprehensive views of natural phenomena, and endowed with a microscopical faculty of seizing and analysing constituent parts and bearings."

We cannot be reminded too often that the really great men are not the great experimenters, nor the great observers, nor the great readers, nor the great scholars, but the great thinkers. Thought is the creator of all human affairs. Actions, facts, and external manifestations of every kind may triumph for a while, but it is the progress of ideas which ultimately determines the progress of the world.

The Influence of Mrs. Hunter on Her Husband's Work and Social Status

It is axiomatic that a wife may either make or mar her husband's career. Many of our most eminent medical men owe advancement in the science and art of their profession to a co-operative and understanding wife. In 1771 John Hunter married Anne Home, the daughter of an Army surgeon. She was 29 and he was 43 years old. She was a very accomplished and charming lady intellectually, and a great social asset. The marriage was not quite in accord with his bachelor brother William's views. For William, a wife who had no dowry was to his mind a pure mistake for a poor man, however great might be her beauty and her ability to lead and shine in society. But John Hunter had good taste. He was by nature an artist and loved pictures above everything ; how then could he fail to desire that the choicest picture in his house should be the most lovely ?

She was a good wife—devoted to her husband and fond of gay society, a taste which occasionally interfered with her husband's more philosophical pursuits. He was so wrapped up in his work that she must have had a lonely time, and must have been thrown much on her own resources. They lived first in Jermyn Street, in a house which his brother William had recently vacated. Later on they moved to a house at the north-east side of Leicester Square, where the Odeon Theatre now stands. Here Mrs. Hunter held her parties, which included many celebrities of the day.

Hogarth was a neighbour ; Sir Joshua Reynolds lived in the precincts, as also Haydn during his first visit to London in 1782. Mrs. Hunter had many friends, among whom were Mrs. Thrale ; Elizabeth Montagu, who was one of the original "blue-stockings" ; and Fanny Burney, the novelist and authoress. Fanny Burney's first and best novel was *Evelina*, published in 1778. Samuel Johnson was her friend and admirer. It is said that Burke sat up all night to read *Evelina*, and that Reynolds would not touch his food until he had reached the end.

The management of the house in Jermyn Street must have often taxed the patience of Mrs. Hunter. Her husband invaded the rooms with his specimens, and the place became a veritable natural history museum. On one occasion Hunter was given a giraffe, and as he could find no room to contain it he cut off its legs and fixed it in the passage. Anne Hunter must have had an anxious time with a young family and husband who would not take care of himself—with patients coming and going, rooms filled with specimens and artists drawing them ; also resident pupils. Holidays were spent in the country at Earl's Court. Hunter's "country" box, as he called it, at Earl's Court was a pleasant hour's drive from his home in Leicester Fields. The house stood in its own grounds with a meadow behind it.

Mrs. Hunter made the house beautiful, decorating it partly in the Egyptian style, then a prevailing fashion. The ceiling of the drawing-room was richly ornamented with strange birds, which her husband must have laughed at but never dared to classify. For Hunter the gardens were "zoological gardens" containing both wild and tame beasts: gardens in which he rambled at night studying the ways and manners of the varied forms of life in every detail. In spite of the temperamental nature of her husband, the marriage was a happy one, largely due to the patience and good temper of Anne. Dr. Joseph Adams, in his Life of John Hunter published in 1817, says: "Hunter had the highest of all human gratifications in the wife of his choice, suited to be his companion, and admirably fitted for, because always accustomed to the elevated rank which her husband had attained."

During his visit to London Haydn composed "The Six Canzonettas for the Voice," for which Mrs. Hunter wrote the libretto, and dedicated them to her. Among her verses is the charming song, "My Mother Bids me Bind my Hair," which lives for ever in the setting Haydn gave it. She also wrote the words of Haydn's *Creation*.

FIG. 2.—Mrs. Hunter.

In a letter to James Baillie, his brother - in - law, dated November 25, 1775, Hunter says: "As to myself, with respect to my family, I can only say that I am happy in a Wife, but my children are too young to form any judgment of them. I am not anxious about my children, but in their doing well in the world. I would rather make them feel one moral virtue than read Librarys of all the dead and living languages. You know I am no scholard, therefore do not feel the beauty of language."

John Hunter died in 1793, in poverty, having spent all his income in the development of his museum. His wife lived in penury until the museum was purchased by the Government in 1799, six years after his death. Mrs. Hunter was a widow for 29 years and died in 1821 at the age of 79. She kept her wit and beauty to the end of her days.

The Hunterian Orator of 1821 paid this compliment to her memory: "She had sustained an honourable widowhood, estimable for talents of her own and venerable as the relict of an illustrious husband."

The Hunterian Era

John Hunter lived and practised his art at a remarkable period in the history of England. He came to London in 1748. William Pitt was guiding the destinies of England. Burke came to London soon after Hunter, to study law, but subsequently turned his attention to politics and literature.

This was also the age of the Arts: Gainsborough, Reynolds, and the portrait painters; of Garrick and the stage. It was also an age which included Chippendale and the Adam brothers. It laid the foundations of modern science and modern medicine, in which John Hunter played a notable part.

The eighteenth century marked an era of religious and social reform, due in part to the influence of such men as John Wesley, William Wilberforce, renowned for his great work in the abolition of slavery, and the philanthropist John Howard, especially famous for his labours to secure prison reform.

John Hunter must have been acquainted with all sections of the population of London, both fashionable and otherwise. The body-snatchers sold him bodies for dissection, and the poor thronged the newly founded hospitals. Consumption and fevers of all kinds were rife, especially gaol fever. The Hunterian era marked a period of much-needed improvement in London's sanitation.

At the beginning of the eighteenth century there were only four important hospitals in London: St. Bartholomew's, St. Thomas's, Bethlem, and the Chelsea Hospital for invalid soldiers. By the time Hunter arrived in London five more general hospitals had been founded: Westminster, Guy's, St. George's, the London, and the Middlesex—all within a few years of each other.

The eighteenth century was an age of indifference to infant life. Children often died abandoned in garrets and in the street. Those left to the care of the Poor Law and parish did not long survive the exigencies of treatment. Thanks to the prolonged agitation of a certain Captain Coram for an institution for the care of these unfortunate children, a Charter was obtained from George II. With the help of Handel, Hogarth, and others, Coram witnessed the fruition of his labours, and in 1745 the Foundling Hospital came into being.

The Influence of John Hunter's Associates and Friends

Sampson Handley in his Oration of 1939 showed how "Hunter's mind, in spite of a very superficial education, was developed by his association with great men of his period, such as his brother William, Cheselden, etc." But other factors were at work in addition to those especially related to the science of medicine. I refer to his contemporary associates in other fields, such as art, music, literature, and drama, all of which must have acted as a stimulus to general knowledge and mental alertness. Time will only permit reference to a few of those whose names are household words:

David Garrick, a famous actor and playwright—friend and pupil of Samuel Johnson. Garrick came to London with Dr. Johnson about 1737. He studied at Lincoln's Inn and also set up in the "wine trade" with his brother for a time, but soon gave up both these activities for the stage. It is worthy of note that in 1769 the Town Hall at Stratford-on-Avon was dedicated by Garrick to the memory of Shakespeare.

Samuel Johnson, author, who acquired a position in literary and artistic circles that has rewarded the efforts of no other man. He was the acknowledged dictator of the Literary Club, founded in 1763 by himself and Sir Joshua Reynolds, and numbering among its limited membership Burke, Boswell, Garrick, Gibbon, Fox, Sheridan, Goldsmith, and others. Boswell's *Life of Johnson*, long accepted as the greatest portrait ever written, was published in 1791.

Richard Brinsley Sheridan, dramatist and politician. He was considered a dunce by his mother at the age of 7. He had an indifferent record at Harrow and cared nothing for scholastic honours. In this respect the background is similar to that of John Hunter in his early days.

Handel, who numbered Pope, Fielding, and Hogarth among his closest friends. The year 1742 witnessed the production in Dublin of that great oratorio the *Messiah*.

All these men and many others were friends and acquaintances of John Hunter and must have had a salutary influence on his line of thought and intellectual make-up, and indirectly in the development of the science and art of surgery.

Hogarth was a neighbour of John Hunter when he resided in Leicester Square. From 1749 to 1764 Hogarth lived at Chiswick, and a mulberry tree grew in his garden. It was his custom to gather local children around him under the tree and feed them with his fruit. The house and tree were badly damaged by enemy action in 1940. The tree had recently fruited for the first time after a number of years. At the reopening of the former house of this great painter at the

beginning of 1952, a small pie, made from the fruit of Hogarth's mulberry tree, now 300 to 400 years old, was given to each guest.

Hunter as Writer and Lecturer

Hunter has been portrayed as "extremely industrious but a poor lecturer, and never had many pupils." As a lecturer, he stressed the advantages derived by a man of putting his thoughts in writing. He resembles, he said, "a tradesman taking stock, without which he never knows either what he possesses or in what he is deficient." A consciousness of the difficulty in making himself understood might have been among the motives for writing his lectures. Convinced of this difficulty in making others understand what appeared simple to himself, he encouraged conversations with his hearers after each lecture, in order to ascertain that his remarks had been clearly expressed. Hunter always professed his lectures to be on "Practical Surgery, with so much physiology as was necessary to render them perspicuous."

Hunter was not a prolific writer. His first appearance as the author of a comprehensive work was comparatively late in life, in 1771, when he was 43 years of age. In this year he published a "Treatise on the Teeth"—a treatise, it has been said, that was forced out of him in order to defray from its sale the expense of his impending marriage. He wrote a number of medical essays. His "Treatise on the Blood, Inflammation, and Gun-shot Wounds," a work dedicated to the King, was his last, and considered by some the greatest of all the Hunterian works.

In a study of Hunter's writings it is often difficult to grasp his line of thought completely. He observed so many things, held such breadth of view, and tried to compress so much into so little, that even had he possessed the necessary skill in exposition he would have been hard to follow. It is, I think, honest to say that, easily as he acquired knowledge from nature, he was according to ordinary ideas an illiterate man, He read from nature and took no time to read from any other source. The principal monument of Hunter's life was his Museum, so aptly described by Professor Wood Jones as "John Hunter's Unwritten Book." He sought truth fearlessly and the search cost him his life. He taught it as he saw it—earnestly, simply, and directly. His influence on medicine and natural science was far-reaching. Ottley, in his *Life of Hunter*, says: "In his writings we occasionally find an obscurity in the expression of his thought, a want of logical accuracy in his reasonings, and an incorrectness in his language, resulting from a deficient education." John Hunter was a poor lecturer and a man of few words. His power of imparting knowledge was chiefly by means of dissections and specimens, but also by sketches. He maintained a resident artist, who was kept busy making drawings of specimens. William Bell was the artist for fourteen years, and William Clift followed him and remained with Hunter to the end.

Hunter as Observer

As an original investigator, Hunter was one of the most laborious and comprehensive of his period. With regard to experimental work, it must be admitted that many of his experiments were rough, and some inconclusive ones led to incorrect inferences, as, for example, in his argument that the "veins do not absorb." But when he came to anatomy, to the broad outlines of natural history, or to the comprehensive grasp of vital phenomena, he had few equals.

As an instance of John Hunter's powers of observation I would mention the Hunterian specimen, in the Museum, of the "head of a chick at the close of incubation," showing the "shell-breaking knob on the top of the upper mandible." To be accurate, the specimen is that of a gosling. After fulfilling its function of breaking the shell of the egg the knob disappears.

A most interesting account of this "Hunterian Specimen and its Problem" was written by Sir Arthur Keith and published in the *Annals* of the College. He drew attention to the fact that John Hunter was the first English observer to take notice of the horny knob of the chick. Nowhere does John Hunter himself claim this priority.

Hunter was in the habit of enunciating "general principles" and then making his facts fit into the framework. Coming to England he passed 40 years in the heart of the most empirical nation in Europe; a nation abhorring all general principles and proclaiming the superiority of facts and ideas. During his long residence in England he was acted on by two conflicting forces: The country of his birth made him "deductive"; the country of his adoption made him "inductive."

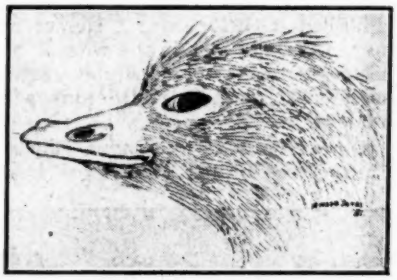

FIG. 3.—Drawing of a specimen prepared by Hunter to show the shell-breaking horny knob on the beak of a newly hatched gosling. By Professor F. Wood Jones. (Hunter's specimen 3456, No. 5, "Young Gosling.")

As a Scot, he preferred reasoning from general principles to particular facts; as an inhabitant of England, he became inured to the opposite plan of reasoning from particular facts to general principles. No doubt one of the reasons why Hunter in investigating a subject is often obscure is that on occasion his mind was divided between these two hostile methods. The conflict darkened his understanding.

Hunter as Surgeon

In *Buckle's History of Civilization*, 1878, it is recorded that Hunter introduced what is probably the most capital improvement in surgery ever effected by a single man—namely, the practice in aneurysm of tying the artery at a distance from the seat of disease—thus saving numerous lives. Before the time of Hunter the operation was performed by cutting into the sac of the aneurysm and tying the vessel above and below. So formidable was this proceeding in its consequences that amputation of the limb was frequently performed as a less dangerous and fatal measure.

As a surgeon, Hunter was a careful if not a brilliant operator; a surgeon who looked upon an operation as the opprobrium of surgery but who did his work well when called upon by necessity. His diagnosis was good for its day, and his observation of phenomena of disease acute. His practical skill was extolled by his former pupil, Astley Cooper. In Brock's recent masterly publication *The Life and Work of Astley Cooper* one realizes the similarity of outlook of master and pupil.

Hunter and the Hunterian tradition were the great inspirations of Astley Cooper's life and work. Hunter, like Astley Cooper, realized the importance of a proper relation between medicine and surgery. Before Hunter's time surgery was held to have but little connexion with medicine.

John Hunter's influence on the development of the science and art of surgery was in the main the natural sequence of his study of the basic sciences of anatomy and physiology, both in health and in disease. His meticulous researches in the realm of morbid anatomy constituted the foundation stone on which he established his *Surgical Principles*. Although the name of John Hunter may not be immortalized as that of a great surgeon, nevertheless he was a great exponent of the art of acquiring knowledge by observation, experiment, and research, without which any advance in surgical procedure is stultified.

Sir Henry Souttar, in his fascinating review of the recently published German book, *Masters of Surgery*, by Professor H. Killian and G. Krämer, lays stress on the brilliant description given of John Hunter as "one whose genius lay in observation and in the elimination of the immature and unscientific; who never wandered in speculation, and whose

whole train of thought was built upon experience." If John Hunter was not a great surgeon he nevertheless was a talented exponent of those sciences which are essential to a sound knowledge of surgical principles and to the making of a surgeon.

Hunter as Pathologist and Museum Builder

Pathology was the science to which Hunter was most devoted. For him pathology was the basis of diagnosis and treatment. His experiments on the healing of wounds are well illustrated in the Hunterian Collection in the Museum of this College. He was a pioneer of the science and art of grafting and transplantation of tissues. His classical and successful experiment of grafting a cock's spur on to its comb is well known. This specimen is preserved in that Collection. He was also interested, and up to a point successful, in the transplantation of human teeth. He wished to study the comparative "growth powers" of different structures and of different situations, since he believed that this had a bearing on disease processes.

Professor Wood Jones, in an address delivered at St. George's Hospital with the title of "John Hunter's Unwritten Book," says: "The collection of specimens constituting the Hunterian Museum is one of the most remarkable monuments that any man has ever raised to perpetuate his memory. His Museum was the medium by which Hunter sought to express those great principles of life which he so profoundly understood, but which neither by speech nor by writing could he make clear to his contemporaries."

Wood Jones emphasizes the fact that John Hunter recognized that, in order to make satisfactory progress in the study of biology, function and structure must be integral parts of such study, and not divorced from each other. This was also in accord with the precepts enunciated and practised by Leonardo, who was designated by William Hunter as the first anatomist of his time.

The Museum

At the time of Hunter's death Clift was custodian of his Museum. The Government offered the executors £15,000 for the whole collection. This was voted by the House in 1799 and was accepted. At this time the collection was still housed at Hunter's residence in Castle Street. The lease of this house came to an end in 1806, when the collection was placed in the custody of the Incorporation of Surgeons—soon to become the Royal College of Surgeons of London and later of England—and was moved to a house in Lincoln's Inn Fields belonging to the College.

FIG. 4.—Samuel George Shattock.

It was largely due to the good offices of William Eden, later to become the first Baron Auckland, a distinguished politician and friend of the Hunters, that after many disappointments the purchase of the Hunterian Collection for the nation was successfully negotiated. He also obtained a government grant for Mrs. Hunter during the first two years of her widowhood. Clift was the first to be appointed Conservator of the Hunterian Collection. He was succeeded by his son-in-law, Richard Owen. Great advances were made under Owen's direction and subsequently. It remained for Sir Arthur Keith, anthropologist and comparative anatomist, to bring the augmented Hunterian Collection to its zenith as the most important of its kind in existence. Trustees were appointed to guard the Hunterian Collection. These have in succession carried on the good work and have co-operated with the Council of the College in the care of the specimens.

Amongst the events which have shaped the design and destiny of the Museum of the College, one of the most important was the engagement of James Paget, in the beginning of 1842, to prepare a catalogue of its pathological collection. An event of equal if not greater moment was the appointment of Samuel George Shattock to the office of Pathological Curator in 1897. The office was then comparatively new. In 1881, while Sir James Paget, assisted by Sir James Goodhart and Mr. Alban Doran, was preparing a second edition of the Pathological Catalogue, the Council decided to appoint a special officer to take charge of the pathological collection. The first occupant of the post was Sir Frederick Eve, then a young surgeon with a special knowledge of tumours. He was succeeded in 1890 by Mr. James Targett, a young gynaecological surgeon with a knowledge of pathological processes. To this office Mr. Shattock was appointed in 1897 as a successor to Targett. He was then 45 years of age, and in the plenitude of his powers.

Hunterian Pictures in the Museum Collection of the College

Certain pictures in the Museum of the College were part of the original Hunterian Collection and illustrate subjects in which Hunter was especially interested. William Bell and John André were accomplished artists, and most of the original drawings in the Hunterian Collection are by them. Several were painted for John Hunter by Zoffany, William Hodges, Stubbs, Robert Home (Hunter's brother-in-law), and William Cheselden. Amongst the collection is a drawing of William Hunter's dissecting-room by Rowlandson.

A number of the pictures have been reconditioned, thanks to the good offices of Geoffrey Keynes, who is "Curator of Portraits and Works of Art" of the College. The beneficial effect of such restorative processes is well shown in some of the famous paintings by Stubbs in the possession of the College, and which were exhibited in the Stubbs Collection at Liverpool in 1951.

The contemporary science of art in Hunter's time, of which he was no mean exponent, must have influenced his surgery and surgical technique. John Hunter showed his artistic temperament by making beautiful dissections.

Medical Societies

John Hunter was a source of inspiration in connexion with metropolitan medical societies. In 1783, together with Dr. George Fordyce, he founded the Society for the Improvement of Medical and Chirurgical Knowledge. The membership was originally nine, with provision for expansion to twelve. It soon became a dining-club, and was dissolved in 1818.

In 1785 the Lyceum Medicum Londinense was started under the patronage of John Hunter and George Fordyce. It met in Hunter's lecture-room in Castle Street, Leicester Square. There were 350 members. In 1809 its members were transferred to the Westminster Medical Society.

Fordyce wrote a *Treatise on the Digestion of Food*, and was remarkable for his practice of having one meal only in the day, at 4 p.m., but this was gargantuan, and went on for an hour and a half. It included a pound and a half of rump steak, a bonne-bouche such as half a boiled chicken or a plate of fish, a tankard of strong ale, a quarter of a pint of brandy, and a bottle of port. It is hardly surprising that he suffered from gout. Fond of society, he would dispense with sleep, and sometimes lectured for three consecutive hours without having undressed on the previous night.

In the latter part of the eighteenth century it was customary for medical consultants to visit coffee houses, such as the famous "Saracen's Head," in order to write prescriptions, at half a guinea or a guinea a time, for apothecaries who described the symptoms of their patients—a somewhat dubious and risky business, but a common and profitable practice among the more noted consultants of the faculty.

Activities of the College

Many of the activities of this College have their roots in the soil prepared by John Hunter and are products of the Hunterian era. First the Museum, the history and functions of which were so clearly enunciated by Professor Grey Turner in his Hunterian Oration of 1945, in which he showed the steps by which the Hunterian Collection grew into the Museum of the College. The name of George Grey Turner is held in esteem and affection by our College. Surely the mantle of Hunter fell on the shoulders of Grey Turner, who was a true disciple of that great man and a worthy exponent of the Hunterian tradition and all that it stands for.

With the growth and rehabilitation of our Museum after its war injuries, it is hoped that the underlying principles of Hunter's teaching will be fostered and the Hunterian tradition of experiment and research maintained.

This is an age of "ideology," but the practical application is not always easy to attain. The "Graphic Museum" in Khartoum is a modern concept of John Hunter's principles of imparting knowledge by a study of all aspects of disease —anatomical, physiological, and pathological. This is achieved by an orderly series of photographs, drawings, and specimens grouped together. It is possible, by spending an hour or so in a small division or alcove of the Graphic Museum, to obtain a shrewd insight into the aetiology, clinical manifestations, complications, morbid anatomy, and treatment of the particular disease in question. After a visit to that Museum one is struck with the possibilities, in any Museum, of such a comprehensive method of instruction.

Research

In 1931 Sir Buckston Browne, one of the greatest benefactors in the history of the College, presented the College with an "Institution of Surgical Biological Research" in a building adjoining the grounds of Downe House, Kent. In a letter to the Council of the College Sir Buckston said: "We all know that John Hunter had a farm at Earl's Court, where, from close observation of living animals, he was able to make his most important additions to surgical knowledge. It is such a farm that I wish the Royal College of Surgeons to accept." The farm is under the able directorship of Sir Arthur Keith, who has been Master of the Research Farm since its inception. The Hunterian tradition of experiment and research has thus been rendered a practical proposition, with notable advances in physiology, technique, and elaboration of surgical principles. It is of historical interest to recall that in 1928 Sir Buckston (then Mr. Buckston Browne) purchased Darwin's home at Downe, and conveyed the entire property to the British Association for the Advancement of Science, to be maintained for all time as a memorial to Darwin.

Hunter had wide vision as regards scientific problems. He could foresee a study of the basic sciences of anatomy, comparative anatomy, and physiology, and their practical application, taken in conjunction with that of morbid anatomy or pathology, culminating in a sound knowledge of the art and science of surgery.

This College has proved its adherence to the Hunterian precept of education in the basic sciences by the inauguration of an Institute of Basic Medical Sciences. By this means co-ordination with the University of London has been effected. Thus the Institute is at the same time both a Faculty of the College and an Institute of the British Postgraduate Medical Federation. The Institute of Basic Medical Sciences is responsible for the teaching of anatomy, applied physiology, and pathology in the College under the able guidance of the Dean, Professor Geoffrey Hadfield. Arrangements are being made to form a department of pharmacology, which will also be administered by the Institute.

One of the more recent activities of the College is the institution of a Clinico-Pathological Research Unit in connexion with the Imperial Cancer Research Fund. The Fund, which is a worthy exponent of the Hunterian tradition of experiment and research, celebrated its jubilee last year.

In 1951 the Council of the College, in their wisdom, initiated a Clinico-Pathological Research Unit, with a view to correlating both the clinical and pathological aspects of research. The new department, established in the precincts of the College, is working in conjunction with experimental research carried out at the Fund's laboratories at Mill Hill. The institution of the Clinico-Pathological Unit is in accordance with Hunterian precepts, and marks a milestone in scientific procedure.

An Academy of Medicine

Sir Max Page, in his Hunterian Oration of 1951, envisaged the formation of an "Academy of Medicine." Previous Orators, notably Victor Bonney, have laid stress on the advantages which might accrue from the integration in one corporate body of the various specialties into which medicine of to-day is breaking up. Such an ideality is ever present in the minds of men of vision. There may be difficulties in bringing this Utopian project to fruition, but the formation of an Academy of Medicine or Mecca of Medical Science in London, by cohesion of the three Royal Colleges, together with their Associated Faculties, and under one roof, is an ideal worth striving for. To my mind such a scientific combination would be for the benefit of each and all concerned, as also of medicine in general. Some members of the profession may be sceptical and inquire, "How do you know that such a symbiosis of the Royal Colleges would advance the science and art of medicine?" I feel sure that if John Hunter were living at the present time he would have a ready answer to this query—namely, "Why not try the experiment?"

Hunter's Death and Commemoration Service

John Hunter at the time of his death was in his 65th year, the same age at which his brother William died. Such was the end of two brothers who, in their own Museums, erected their own monuments. Both arrived in London with no capital but genius, industry, and integrity. Each arrived nearly at the same age, finished his career in the same time, and each in the arena of his own labours: William struck with approaches of death in his own theatre, and in his expiring moments anxious to return that he might communicate a physiological fact he never could ascertain till then—namely, "How pleasant a thing it is to die"; John expiring on the spot. To set the time of John Hunter's death by the course of history Clift wrote this title on his account-book:

> John Hunter, Esq., F.R.S.,
> Surgeon-General to the Army and
> Inspector-General of Hospitals.
> Surgeon to St. George's Hospital.
> Surgeon-Extraordinary to the King.
> etc. etc. etc.
> Died October 16th 1793.

On the same day, and perhaps hour, the unfortunate Marie Antoinette, Queen of France, was beheaded in Paris.

John Hunter was buried in St. Martin-in-the-Fields Church. In 1859, when the coffins in the vaults of St. Martin's were moved for reinterment, Frank Buckland, a Member of this College, undertook the task of finding Hunter's body. He began on January 26, and searched for 16 days, by which time he had viewed 3,060 coffins; then he found it, when only three still remained for him to examine.

On March 28, 1859—that is 66 years after Hunter's death—his remains were reinterred in the north aisle of Westminster Abbey. A brass tablet in the stone floor of the nave of the Abbey, placed there by the Royal College of Surgeons of England, records the admiration of the College for :

> "His genius as a gifted interpreter of the Divine Power and Wisdom at work in the laws of Organic Life, and their grateful veneration for his services to mankind as the Founder of Scientific Surgery."

The statue of John Hunter in the Museum of the College was erected by subscription on the occasion when John Hunter's remains were transferred to Westminster Abbey, in 1859. The statue is the work of Weeks, and is a copy in marble of the celebrated picture of John Hunter by Sir Joshua Reynolds in the Council Room of the College.

On February 14, 1952, Hunter's birthday, a service was held at St. Martin-in-the-Fields to commemorate the fact that John Hunter was buried in the church until 1859, when his remains were removed to Westminster Abbey. The service was conducted by the Dean of Westminster; the lesson read by the President of the Royal College of Surgeons, Sir Cecil Wakeley; and an address given by Sir Gordon Gordon-Taylor. A plaque was set up in the crypt, and was unveiled by Sir Henry Dale, a Hunterian Trustee. The plaque, besides recording the facts of Hunter's interment and reinterment, commemorates the name of Frank Buckland, the discoverer of the Hunter coffin. As Sir Gordon Gordon-Taylor remarked in his address: "It was owing to the zeal and enthusiasm of the late George Grey Turner that the project to place the plaque in the church had come to fruition."

On the front page of a brochure which deals with the restoration and development of the Royal College of Surgeons of England, the following lines appear: "All through the ages a golden truth is blazoned; the path of Progress is by Experiment, Research, and Trial." Surely here is the essence of the Hunterian tradition, of which the Royal College of Surgeons of England is the custodian.

TREATMENT OF PATIENTS WITH MYELOSCLEROSIS

BY

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Unless new bone formation in the marrow spaces has occurred (osteosclerosis), which can be detected by *x*-ray examination, the presence of fibrosis of the bone marrow can be proved in life only by biopsy of a bone in which red marrow is normally present. Needle puncture of the sternum and other bones is not a reliable method of detecting the presence of fibrosis. Bone-marrow cells are usually present among the fibrous tissue or in spaces lined by endothelium in the fibrous tissue, and the fibrosis may be patchy, and an active portion of bone marrow may be encountered. When the fibrosis is very dense, however, few bone-marrow cells may be present.

The object of this paper is to draw attention to the good results which may be obtained by *x*-ray treatment in certain cases, results comparable to those obtained in treating typical cases of chronic myeloid leukaemia (chronic leukaemic myelosis). Some recent writers, assuming that the enlargement of the spleen is a compensatory process to replace the fibrous bone marrow, have stated that *x*-ray treatment is harmful (Levinson and Limarzi, 1947; Paolino, 1949; Wyatt and Sommers, 1950).

Rarely patients with myelosclerosis may have the changes in the circulating blood of polycythaemia (Hirsch, 1935; Vaughan and Harrison, 1939; Sussman, 1947; Marson and Meynell, 1949, 1952) or of myeloid leukaemia (Heuck, 1879; Rosenthal and Erf, 1943; Sussman, 1947), but more commonly the changes are those of anaemia. Rarely the patient may die, within a few months from the first symptoms, of severe anaemia, with haemorrhages into the skin and from mucous membranes, presenting a clinical picture like that of acute or subacute leukaemia (Assmann, 1907; Mozer, 1927; Wood and Andrews, 1949). But most patients with myelosclerosis have splenomegaly, slight or no anaemia, with an increase in circulating leucocytes of varying degree and varying proportions of immature leucocytes and nucleated red cells. The enlargement of the spleen is due to myeloid metaplasia, usually involving granulocytes, nucleated red cells, and megakaryocytes. The megakaryocytes are often the most prominent cells in the myeloid metaplasia, partly because of their size and the ease with which they are recognized ("megakaryocytic myelosis").

When severe anaemia is present blood transfusion is the best treatment, and some patients have been kept alive for many years by repeated transfusions (Collins, Sanger, Allen, and Race, 1950). Some patients, however, do not respond to blood transfusions, and these may die of severe anaemia after a short illness. The anaemia does not respond to iron by mouth, or to liver extract by mouth or by injection. But most patients with myelosclerosis live a long time, and in these spontaneous remissions from anaemia may occur, and even polycythaemia may develop (Windholz and Foster, 1947; Hutt and Richardson, 1950).

The patients with myelosclerosis who have either no anaemia or only slight anaemia usually seek advice because of symptoms due to the large spleen. They may, however, have severe gastro-intestinal haemorrhages and large haemorrhages into the tissues, usually have cramps in the legs at night, and may have attacks of gout. Many of these patients ultimately die of severe anaemia, after a long period, but some never develop anaemia throughout and die of weakness and wasting or heart failure.

It is those patients with a high leucocytosis and a high proportion of immature cells in the circulating blood who respond well to *x*-ray treatment, regardless of the degree of myelosclerosis.

In many of these patients the main trouble is abdominal discomfort due to the large spleen; the general health of the patient may be unaffected, and he may be able to lead an active life consistent with his age. In such cases no treatment should be given except for encouragement to bear with the abdominal symptoms, some relief from which may be given by an abdominal supporting belt. Later on symptoms of general ill-health may occur, such as tiredness, weakness, and, later still, wasting. The first course of *x*-ray treatment produces the best result, and should be postponed until either severe abdominal symptoms or general symptoms of ill-health occur. This may produce a very good result, the abdominal symptoms diminishing or disappearing as the spleen decreases in size—weakness, tiredness, and cramps in the legs disappearing, and the patient being enabled to lead an active life again. This result is accompanied by a decrease in the numbers of the circulating leucocytes and of the immature leucocytes and nucleated red cells, and a decrease in numbers

of basophils and eosinophils if these were previously abnormally high. The improvement in the patient's condition lasts varying periods of time, as in typical cases of chronic myeloid leukaemia. Courses subsequent to the first usually produce diminishingly good effects.

Present Series

These observations are based upon four patients with osteosclerosis, and five patients with myelosclerosis without demonstrable *x*-ray changes in the skeleton, who have been under my care. One patient with osteosclerosis is still living. Of the eight who have died, full post-mortem examinations were made upon seven. In the other case, one of advanced osteosclerosis that was under observation from 1923 to 1938, only the spleen and liver were examined at necropsy.

Of these nine patients, seven had *x*-ray treatment, either to the spleen alone or to the spleen and long bones. One patient had severe anaemia when first seen; there was no increase in circulating leucocytes, though immature leucocytes, nucleated red cells, and megakaryocytes were present (the last up to 21% of the circulating leucocytes). Her response to blood transfusions was poor. Two injections of nitrogen mustard did no good, and she died four months after she was first seen. The remaining patient appeared as a case of acute leukaemia, with severe purpura, severe anaemia, slight leucopenia, immature leucocytes, and nucleated red cells in the circulating blood; he showed poor response to blood transfusions, and died two weeks after he was first seen and five months after the first symptoms of ill-health.

Of the seven patients who had *x*-ray treatment, two got no benefit. Neither of these had an increase in circulating leucocytes. One died of severe anaemia after five years' observation, during most of which time she had been able to work. Severe anaemia was present only during the last year. The other died of severe anaemia after 16 months' observation. Neither of these two patients responded well to blood transfusions; that is to say, this treatment improved the patient's health only slightly and temporarily.

But the remaining five patients got great benefit from *x*-ray treatment. They all had a large increase in circulating leucocytes, 20,000 to 70,000 per c.mm. before *x*-ray treatment. One, a patient with advanced osteosclerosis, was under observation from 1923 to 1938, and died of heart failure, never having severe anaemia throughout. He had a short course of *x*-ray treatment to the spleen in 1936, which decreased the discomfort due to the large spleen. Another patient, with early osteosclerosis, is still living. He has been under observation from early 1949 until the time of writing. A course of *x*-ray treatment to the large spleen in July, 1952, greatly improved his feeling of well-being, relieved the severe abdominal symptoms, and stopped the cramp in the legs.

The remaining three patients had more than one course of treatment. One, a patient with advanced osteosclerosis, *x*-ray pictures of whose bones have been published (Hickling, 1937), had *x*-ray treatment in 1938, 1939, and 1941. The first two courses produced very good effects upon her general health and upon the abdominal symptoms. The last course produced much less effect, and she died of severe anaemia in 1942, after five and a half years' observation. Severe anaemia was present only during the last year of her life, and did not respond well to blood transfusions. A series of *x*-ray pictures of this patient's bones was made, and the degree of osteosclerosis appeared to diminish after the first course of *x*-ray treatment.

Another patient, with myelosclerosis, without *x*-ray changes in the bones, had three courses of *x*-ray treatment, in 1948, 1949, and 1950. This man's chief trouble was repeated severe gastro-intestinal haemorrhages. He died after four years and four months' observation. The first two courses of *x*-ray treatment improved his feeling of well-being and diminished the abdominal discomfort, but did not seem to diminish his tendency to gastro-intestinal haemorrhages.

The other patient had seven courses of *x*-ray treatment, to the first four of which his response was very good, though each course brought on an attack of gout, which started eight years before the first course of *x*-ray treatment. He died in 1945, of weakness, wasting, and chronic gout, after six and a half years' observation.

Discussion

A course of *x*-ray treatment should be planned so that just enough is given to relieve abdominal symptoms due to the large spleen. This also has the effect of relieving such general symptoms as tiredness, weakness, and cramps in the legs. If more than this is given, anaemia and leucopenia may occur. Two patients developed leucopenia as a result of too much *x*-ray treatment—one after the first and only course, and the other after the third course. In neither case did the leucopenia do any apparent harm. One patient developed anaemia after a course of *x*-ray treatment, which otherwise produced a good result, and slow recovery from the anaemia occurred.

Though many writers state that *x*-ray treatment of patients with myelosclerosis is harmful, some have reported good results (Reiche, 1927; Dameshek, 1945; Marson and Meynell, 1952; Nelson, 1952).

Most writers have taken the view that the myeloid metaplasia of the spleen and other organs is secondary to the fibrous or bony replacement of the bone marrow. Some believe that most cases of osteosclerosis or myelosclerosis are atypical forms of chronic granulocytic leukaemia (Custer, 1949). Others have suggested that myelosclerosis and osteosclerosis may be due to alterations in the undifferentiated cells of the bone marrow, of unknown origin, comparable to the alterations which cause increase in leucoblasts and erythroblasts (Vaughan and Harrison, 1939; Merskey, 1949; Moeschlin, 1951; Robson, 1952). The reduction in the degree of osteosclerosis of one of my patients under *x*-ray treatment supports this view, if it can be confirmed in other cases.

Splenectomy was not performed on any of the nine patients. Some authorities believe that occasionally this operation might do good (Bodley Scott, 1952; Richardson, 1952). References have been found to 14 patients with osteosclerosis or myelosclerosis who had splenectomy (Nauwerck and Moritz, 1905; Hirschfeld, 1914; Mettier and Rusk, 1937; Carpenter and Flory, 1941; Reich and Rumsey, 1942; Hittmair, 1944; Crail, 1946; Heller, Lewisohn, and Palin, 1947; Dustin, 1947; Crail, Alt, and Nadler, 1948; Wyatt and Sommers, 1950; Franks and Richardson, 1952). Of these 14 patients, four died within three months and four between ten months and six and a half years after splenectomy. Of the six recorded as having survived splenectomy, two survived a short time and four survived between one and five years. No striking improvement was produced in the condition of any of the patients, except one (Franks and Richardson, 1952). This patient was living several months after splenectomy and did not need the very frequent blood transfusions previously required.

Case Reports

Case 1.—A man aged 71. Presenting symptom, hardness of abdomen, and large spleen found February, 1949. No anaemia, no polycythaemia. Leucocytes 26,000 per c.mm., 10% immature cells. Cramps in legs since 1947. General health good for his age. *X*-ray pictures of skeleton show early osteosclerosis, mainly of humeri. Sternal marrow active, all elements involved, many whole and fragmented megakaryocytes. *X*-ray treatment to spleen, July and August, 1952; spleen reduced in size, cramps in legs disappeared. Slight anaemia resulted, which gradually disappeared. In good health for his age, February, 1953.

Case 2.—A woman aged 65 died in December, 1951, of weakness, wasting, and heart failure, after five years' obser-

vation. Presenting symptom, thrombosis of ventral vein of retina, December, 1946; enlarged spleen found. Slight anaemia, leucocytes 4,600 per c.mm., 19% immature cells. Spleen gradually increased in size, cramps in legs started in 1950, but she worked until April, 1951, when she became weak and ill. Sternal puncture failed to produce marrow cells. Trephine biopsy of sternum showed advanced myelosclerosis. No *x*-ray changes in bones. After April, 1951, blood transfusions, liver by mouth and by injection, cortisone and *x*-ray treatment to spleen were all ineffective. *Necropsy:* Intense myeloid metaplasia of spleen, Malpighian bodies little affected, many megakaryocytes; slight myeloid metaplasia of liver; intense myeloid metaplasia of some lymph nodes; intense fibrosis of marrow of sternum, humerus, femur, ribs, and vertebral bodies.

Case 3.—A man aged 51 died of weakness and wasting, July, 1950, after four years and four months' observation. Presenting symptom, severe intestinal haemorrhage, March, 1946, when a large spleen was first found. These haemorrhages occurred at intervals from 1942 to 1949. Spleen gradually increased in size until 1948, when it reached beyond the midline. No polycythaemia. No anaemia, except after haemorrhages. Leucocytes 15,000 to 24,000 per c.mm., immature cells 8 to 12%, megakaryocytes 1.5 to 2.2%. *X*-ray treatment December, 1948, caused shrinkage of spleen, decrease in total leucocytes, and percentage of immature cells. Second course in June and July, 1949, again produced improvement. Sternal marrow puncture produced a fluid poor in cells, in which megakaryocytic nuclei and other marrow cells can be seen. A third course of treatment in June, 1950, did no good. *Necropsy:* Intense fibrosis of marrow in sternum, humerus, and femur, but marrow cells recognizable among the fibrous tissue. Myeloid metaplasia of spleen, very few and small Malpighian bodies; very slight myeloid metaplasia of liver; four ulcers, recent in origin, in jejunum.

Case 4.—A man aged 49 died of weakness, wasting, and anaemia in June, 1945, after six and a half years' observation. Presenting symptom, abdominal discomfort, and large spleen found, January, 1939. Attacks of gout since 1931. Cramps in legs since 1938. Bone *x*-ray pictures normal. No anaemia. Leucocytes 38,400 per c.mm., immature cells 13%, nucleated red cells 3% of total nucleated cells in circulating blood. Sternal marrow active, May, 1943. *X*-ray treatment 1939, 1940, 1941, 1942. The first three courses produced very good results, the spleen shrinking, leucocytes diminishing, general health improving, and cramps in the legs disappearing. In 1943 weakness and wasting occurred, and anaemia, which did not respond well to blood transfusions. *Necropsy:* Fine fibrosis of marrow of sternum, ribs, and humerus, with spaces lined by endothelium packed with marrow cells, including large numbers of megakaryocytes. Myeloid metaplasia of spleen, with megakaryocytes; intense myeloid metaplasia of liver; few scattered areas of myeloid metaplasia in kidneys.

Case 5.—A woman aged 67 died of anaemia and heart failure in January, 1949, after five months' observation. Presenting symptoms, weakness and abdominal pains, September, 1948; anaemia and a large spleen found. Circulating leucocytes 8,000 per c.mm., of which 12% were immature cells; 5% of nucleated cells were erythroblasts, and 4% megakaryocytes. Bone *x*-ray pictures normal. Sternal marrow puncture produced a fluid poor in cells, among which megakaryocytic nuclei were prominent. Poor response to blood transfusions. Megakaryocytes in circulating blood later rose to 21%. Two injections of nitrogen mustard did not help. *Necropsy:* Dense fibrosis of marrow of humerus and sternum, no myeloid metaplasia of liver, intense myeloid metaplasia of spleen, megakaryocytes not conspicuous.

Case 6.—A man aged 71 died of weakness, wasting, and heart failure in March, 1938, after fifteen years' observation. Presenting symptom, abdominal pains, 1923, and large spleen found. No anaemia, no polycythaemia. Leucocytes 16,000 per c.mm.; 31% immature cells, and 4% erythroblasts. No bone *x*-ray pictures until 1936, when extensive advanced osteosclerosis was found. Cramps in legs 1936 onwards. No treatment until 1936, when spleen extended nearly to the right anterior superior iliac spine. *X*-ray treatment caused some shrinkage of spleen. Leucocytes rose greatly at end, being between 40,000 and 90,000 per c.mm., from 1936 to 1938, with monocytes 12 to 25%. *Necropsy:* No other disease found, but only spleen and liver available for section. Intense myeloid metaplasia of spleen, mainly composed of one type of cell, Malpighian bodies absent; intense myeloid metaplasia of liver.

Case 7.—A woman aged 66 died of weakness, wasting, and anaemia in February, 1942, after six and a half years' observation. Presenting symptom, abdominal pains, 1935, and a mass felt in abdomen. At operation, performed on incorrect diagnosis, the mass was found to be a large spleen; a spleniculus was removed for histology. Leucocytes 30,000 per c.mm., 18% immature cells. Cramps in legs 1939–42. Bone *x*-ray pictures, 1936, showed advanced osteosclerosis. *X*-ray treatment to spleen and long bones 1938, 1939, 1941. The first course produced excellent results, spleen shrinking, general health improving, and serial *x*-ray pictures of bones showed diminution in intensity of osteosclerosis, especially after the first course. The second course also did good, the last was ineffective. *Necropsy:* Dense osteosclerosis of sternum, humerus, femur, ribs. Intense myeloid metaplasia of spleen, no visible Malpighian bodies. The spleniculus removed in 1935 showed myeloid metaplasia of pulp, with unaffected Malpighian bodies. Moderate myeloid metaplasia of liver. Intense myeloid metaplasia of lymph nodes from different areas and of lymph tissue in appendix.

Case 8.—A man aged 61 died of wasting, weakness, and anaemia, November, 1940, after one year and four months' observation. Presenting symptoms, tiredness, and irritability of legs, but rarely cramps. Moderate anaemia, total leucocytes normal, constant presence of immature cells and erythroblasts. Bone *x*-ray pictures normal. Iron and liver extract by mouth were no help. *X*-ray treatment produced very slight improvement in his health, spleen shrank considerably. Later, blood transfusions produced transient improvement only. *Necropsy:* Fine fibrosis of marrow of sternum and humerus, with endothelium-lined spaces packed with marrow cells; megakaryocytes plentiful. Myeloid metaplasia of spleen; Malpighian bodies not affected. Slight myeloid metaplasia of liver.

Case 9.—A man died of severe anaemia, June, 1952, after two weeks' observation. Presenting symptom, severe arthritis of hands, May, 1952. Moderate enlargement of spleen, purpura of legs and mucous membrane of mouth, severe anaemia, slight leucopenia, immature leucocytes 8%, nucleated red cells 36%. Serum uric acid 8.3 mg. per 100 ml. Sternal marrow puncture produced very few marrow cells. Poor response to large blood transfusion. *Necropsy:* Dense osteosclerosis of sternum and humerus, with practically no marrow cells visible; myeloid metaplasia of liver, spleen, and spleniculus; Malpighian bodies present but small; megakaryocytes not conspicuous.

Summary

A brief account is given of the chief clinical features of patients who have sclerosis of the bone marrow.

Those patients who have large numbers of leucocytes in the circulating blood, with immature cells among them, respond well to *x*-ray treatment, regardless of the degree of marrow sclerosis.

Serial *x*-ray photographs of the bones of one patient, before, during, and after *x*-ray treatment, were taken by Dr. W. H. Coldwell. Sir Alun Rowlands and Professor Clifford Wilson allowed me to see patients with myelosclerosis under their care. I am grateful to these gentlemen for their help.

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POLYCYTHAEMIA, LEUCO-ERYTHROBLASTOSIS, AND MYELOSCLEROSIS

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Reduction or obliteration of the bone marrow by connective-tissue proliferation or increased formation of bone occurs in the hereditary childhood condition of osteopetrosis, or marble bone disease of Albers-Schönberg, and also in a non-hereditary adult condition. This latter is probably best known as myelosclerosis, in which myelofibrosis or ossification of the marrow, sometimes called osteosclerosis, may be the predominant feature. The blood picture characteristically accompanying this condition shows leuco-erythroblastosis—defined by Vaughan (1936a) as "an anaemia characterized by the presence in the peripheral blood of unusually immature red cells and a few immature white cells of the myeloid series. The anaemia is not necessarily severe, nor is there usually a marked leucocytosis." Previous polycythaemia in cases which eventually showed leuco-erythroblastosis and myelosclerosis has been described by Lehndorff and Zak (1907), Hirsch (1935), Vogel, Erf, and Rosenthal (1937), Stone and Woodman (1938), Rosenthal and Bassen (1938), Markoff (1939), Vaughan and Harrison (1939), Thompson and Illyne (1940), Jackson, Lemon, and Parker (1940), Rosenthal and Erf (1943), Stealy and Sumerlin (1944), Windholz and Foster (1947), Marson and Meynell (1949), Merskey (1949), Wyatt and Sommers (1950), and H. N. Robson (personal communication, 1952).

We are here reporting three further cases presenting as polycythaemia and terminating as leuco-erythroblastic anaemia and myelosclerosis.

Case 1

A 69-year-old woman, first seen in May, 1946, complained of pain in the lumbar region and in the hips and calves for one year and an aching mass in the left side of the abdomen for five months. Examination revealed a malar flush with slight cyanosis, a moderately enlarged heart, splenomegaly extending down to the symphysis pubis and across to the right side of the abdomen, and slight hepatomegaly. A blood count showed: red cells, 5,920,000 per c.mm.; Hb, 113%; white cells, 11,600 per c.mm. (premyelocytes 1%, myelocytes 8%, metamyelocytes 4%, neutrophils 68%, eosinophils 3%, basophils 2%, lymphocytes 11%, monocytes 3%); 2 nucleated red cells per 100 white cells; and some polychromasia. Achlorhydria was present, serum calcium was 9.6 mg. per 100 ml., and the Wassermann reaction was negative.

Nearly four years later, in February, 1950, readmission was necessary for pain and weakness of the left leg, frequency and urgency of micturition, and weakness, lassitude, and loss of weight. Ankle oedema with pigmentation and ecchymoses over both legs was present. All other physical signs were unchanged. Liver-function tests and radiographs of the long bones were normal. A blood count showed: red cells, 3,100,000; Hb, 66%; white cells 7,000 (myeloblasts 4.5%, premyelocytes 0.5%, myelocytes 6%, metamyelocytes 0.5%, neutrophils 56%, eosinophils 0.5%, basophils 5%, lymphocytes 16.5%, monocytes 8.5%, atypical monocytes 1.5%, mitotic figures 0.5%); 14 nucleated red cells per 100 white cells; and some macrocytosis. A biopsy of sternal marrow showed myelofibrosis; the haemopoietic tissue was almost entirely replaced by fibrous tissue; of the cellular elements megakaryocytes were present in increased numbers; polymorphonuclear cells with a small number of normoblasts could be seen scattered amongst the fibrous tissue; no haemosiderin could be detected by Perles's stain.

Case 2

A 48-year-old farmer's wife, when first seen in June, 1937, complained of morning hunger pains and three recent attacks of epigastric pain, backache, and vomiting. Examination showed a plethoric facies, slight sclerotic icterus, and splenomegaly extending 8 cm. below the costal margin. A blood count showed: red cells 8,500,000; Hb, 122%; white cells, 9,100 (neutrophils 92%, eosinophils 2.5%, basophils 1.5%, lymphocytes 2%, monocytes 2%); reticulocytes, 0.5–1%; some macrocytosis and moderate anisocytosis. Barium-meal examination showed only displacement of the stomach to the right. The presumptive diagnosis being polycythaemia vera, the spleen was irradiated, with considerable improvement.

Irradiation of the humeri and femora with reduction in the blood count—which had again risen to red cells, 7,500,000; Hb, 128%; white cells, 7,400—was carried out in February and March 1942. She remained fairly well for over three years, apart from several severe epistaxes in January, 1944, and on July 19, 1945. In January, 1946, treatment was necessary for the anaemia, then present—red cells, 3,200,000; Hb, 60%; white cells, 3,000; subsequently her condition remained stationary for over three years. Further treatment for the anaemia was necessary in August, 1949. The blood count showed red cells, 2,500,000; Hb, 48%; white cells, 4,200 (myelocytes 2%, metamyelocytes 6%, neutrophils 55%, eosinophils 4%, basophils 2%, lymphocytes 29%, monocytes 2%); 12 nucleated red cells per 100 white cells; and 3% reticulocytes. The spleen extended almost into the left iliac fossa and the liver to 9 cm. below the costal margin. Radiographs of the skull, pelvis, and long bones showed no abnormality. The red-cell fragility test showed commencing haemolysis in 0.5%

Sternal Marrow Counts

Cells	Case 1	Case 2	Case 3
Blasts	4·0	3·0	2·4
Premyelocytes	1·0	—	0·4
Myelocytes	22·0	15·0	10·0
Metamyelocytes	11·0	13·0	7·2
Neutrophils	41·0	34·0	39·6
Eosinophils	—	2·0	2·8
Basophils	—	—	2·4
Lymphocytes	1·0	21·0	23·6
Monocytes	4·0	—	—
Normoblasts A	12·0	—	3·2
Normoblasts B		5·0	6·0
Normoblasts C		7·0	1·6
Mitoses	1·0	—	0·4
Megakaryocytes	—	—	0·4
Unclassified	3·0	—	—
Nucleated Cell Count per c.mm.			6,300
Leuco-Erythroid Ratio			1·6 : 1
Comment		A very poor cellular marrow.	Marrow easily obtained, bone not unduly resistant.

saline and completion in 0.35% solution. Sternal puncture revealed a very poor cellular marrow (see Table).

A biopsy was taken from the eighth rib. On section, the outer compact bone formed a thin layer no more than 2 mm. in thickness; the marrow cavity appeared greyish in the preserved specimen; transverse sections showed a notable fibrosis of the marrow spaces in the peripheral zones and a loose-constructed fibrosis, together with adipose tissue in the centre of the medullary cavity; there was no increase in the bony trabeculation of the rib, and, in fact, in many areas giant-cell osteoclasis was active; there was a marked reduction in haemopoietic tissue, which was mainly confined to one or two islets near the rib cortex; the predominant cells seemed to be eosinophil myelocytes; and there were also many eosinophil polymorphonuclears.

Subsequently she was admitted frequently in 1949, 1950, and 1951 for blood transfusion.

Case 3

A foreman engineer aged 51 was seen in March, 1944, complaining of occasional attacks of gout, recent slight loss of weight, and a left subcostal mass present for two years but only recently causing intermittent pain.

Examination showed only moderate enlargement of the spleen. A blood count showed: red cells, 5,600,000, Hb, 120%; white cells, 13,600 (myelocytes 9%, metamyelocytes 3%, neutrophils 45%, eosinophils 1%, lymphocytes 36%, monocytes 6%); 3 nucleated red cells per 100 white cells; and slight anisocytosis. Achlorhydria was present. Radiographs of the chest, lumbar spine, and pelvis revealed no bony abnormalities.

In September, 1945, the spleen extended into the left iliac fossa and the liver was slightly enlarged; few petechiae were scattered over the body. Irradiation of the spleen was carried out then, and in January, 1947, and in March, 1948, his general condition remaining fair. In March, 1949, he had severe perisplenic pain, general weakness, and acute gout. A blood count showed: red cells, 3,400,000; Hb, 64%; white cells, 9,200 (myelocytes 6%, metamyelocytes 15%, neutrophils 66%, lymphocytes 13%); 9 nucleated red cells per 100 white cells; reticulocytes, 3%; bleeding time, 3½ minutes; and clotting time, 5 minutes. The ribs showed an alteration in the bony texture radiologically, but no destructive process was visible. A sternal marrow biopsy showed myelofibrosis; the bony trabeculae were coarse and compactly arranged; the intervening marrow spaces were filled in some areas by adipose tissue, in others by vascular fibrous tissue; islets of haemopoietic cells were few, small, and widely scattered, and in most places were represented by the presence of a few megakaryocytes.

On his last admission, on September 27, 1949, five and a half years after his first appearance, examination showed anaemia, gross splenomegaly, moderate hepatomegaly, ascites, basal pulmonary oedema, and gross oedema of the ankles. Death occurred on October 12, 1949.

Necropsy Findings

The lungs showed oedema with congestion of the lower lobes. The heart was dilated, with a pale greasy myocardium. The spleen weighed 2,330 g. Its capsule showed several large and small white opaque patches. On slicing, no Malpighian corpuscles could be seen. The surface showed a pale brick-red appearance with several irregular haemorrhagic zones of varying size. The liver weighed 4,020 g. Its capsule also showed opaque white patches. On slicing, the surface was paler and the consistency firmer than normal. There was an irregular fine whitish mottling, in parts simulating the nutmeg effect. Both kidneys on section were paler than normal. The gastric mucosa showed haemorrhagic patches. Some haemorrhages were also visible in the bladder.

Histology

Rib.—A section of rib showed pronounced osteosclerosis. Thick bony trabeculae were present. In some parts the trabeculae were very wide and the marrow space very small. The marrow was fatty towards the centre of the bone, but showed prominent fibrous areas with spindle-shaped cells, apparently fibroblasts, and groups of red- and white-cell precursors. The precursors were scanty and patchily distributed. Giant cells of the megakaryocytic type were prominent in some of the fibrous areas.

Vertebral Body.—The most striking changes were the presence of loose fibrous marrow and the sparseness of red- and white-cell precursors. Occasional multinucleated giant cells were visible. In some areas the bony trabeculae were wider than normal, but osteosclerosis was less pronounced than in the rib.

Spleen.—The normal splenic architecture was destroyed. Some increase in fibrosis was present. Malpighian bodies were absent. Numerous precursors of the red and white cells were present. Large cells with convoluted nuclei, some polychromatic and vesicular and others hyperchromic, were prominent in some parts, as many as eleven being in one high-power field. Numerous cells with indented nuclei and an eosinophilic slightly granular cytoplasm were also present.

Liver.—This showed scattered foci of leucopoiesis and erythropoiesis, situated mainly around the central vein. Amongst the cells of the granular and erythrocyte series there were large multinucleated cells similar to those found in the bone marrow and spleen.

Kidney.—Small foci of erythropoiesis and leucopoiesis were present.

Discussion

These cases presented the characteristic symptomatology, splenomegaly, and other physical signs and haematological features of polycythaemia vera, and resembled others described in that the polycythaemic blood-count figures were not very high.

The development of anaemia in the later stages of polycythaemia has often been noted. Minot and Buckman (1923) described a "secondary" anaemia, but the report of immature red and white cells in the blood suggests that this may have been leuco-erythroblastic anaemia. Several other authors have described the development of a typical leuco-erythroblastic anaemia. It is possible that the leuco-erythroblastic state has often been missed, for McMichael and McNee (1936) considered that repeated examination of the blood might be required to detect primitive red and white cells owing to the variations and fluctuations in the haematological features. In Case 2, unlike the others, immature red and white cells were not observed until the anaemic phase. As in the other cases mentioned above, myelosclerosis was found during the period of leuco-erythroblastosis. Recently, however, Hutt (1950) and Marson and Meynell (1952) in two cases discovered fibrosis of the sternal

marrow during actual polycythaemia. Cases of myelosclerosis with leuco-erythroblastic anaemia, but without previously recorded polycythaemia, have been reported by several authors, including Stephens and Bredeck (1933) and Rosenthal and Erf (1943).

A common feature of these cases, both with and without previous polycythaemia, has been the presence of myeloid metaplasia in the spleen. Numerous authors have commented on this—for example, Chapman (1933) found extramedullary hyperplasia of myeloid tissue described in 11 out of 14 reported cases. Askanazy (1904) apparently was among the first to indicate that reticulo-endothelial cells could become blood-forming cells in adults, while Hirschfeld (1905) recognized the importance of this myeloid metaplasia as a unifying feature of the cases. In the metaplasia Carpenter and Flory (1941) pointed out that, "in addition to leucoblastic cells, erythroblasts are constantly prominent and giant cells (megakaryocytes) are numerous." Most accounts, with the notable exception of that of Heller, Lewisohn, and Palin (1947), are in agreement with the view that all haemopoietic tissues are involved.

Vaughan (1936b) summarized 17 cases of myelosclerosis: in only one of the 14 cases in which necropsy or biopsy was performed was no myeloid metaplasia found in the spleen. Stephens and Bredeck (1933) collected 24 cases from the literature—19 of which were complete enough to be tabulated—and found that these latter showed splenomegaly, myelosclerosis, and myelaemia, and all but one showed normoblastaemia.

Despite the frequency of the occurrence together of myelosclerosis, leuco-erythroblastosis, myeloid metaplasia in the spleen, and megakaryocytic prominence in the spleen and marrow, which perusal of the literature reveals, the establishment of the syndrome comprising them has been rendered difficult by different authors emphasizing in their titles various characteristic features in these essentially similar cases.

The Syndrome

The morphological, haematological, and clinical features of this polymorphic leukaemia-like syndrome have been discussed by Heller *et al.* (1947). The condition, they say, is characterized clinically by a slowly progressive splenomegaly occurring in persons of either sex, usually within or beyond the fifth decade of life. There may be little impairment in the general health for many years, following which generalized weakness, anorexia, weight loss, ill-defined aches and pains, and discomfort occasioned by the greatly enlarged spleen frequently occur. The liver may enlarge. As a rule there is no significant involvement of the lymph nodes. The blood picture, according to Carpenter and Flory (1941), displays widely varying conditions from a rare initial polycythaemia to varying grades of anaemia, usually normochromic, but occasionally hypochromic; nucleated red cells have been prominent in all but a few cases. Immature red cells have not been seen in the peripheral blood in some cases—for example, Tudhope (1937) and Heller *et al.* (1947). Macrocytosis has occurred in the cases of Carpenter and Flory (1941), Heller *et al.* (1947), Robson (personal communication, 1952), and our Cases 1 and 2. Lindeboom (1938) thought that polychromasia, poikilocytosis, and anisocytosis were more pronounced in these cases than would be expected for the degree of anaemia.

The total white-cell count, according to Thompson and Illyne (1940), is rarely very high and is almost always well below the levels seen in untreated leukaemia. Myelocytes in the peripheral blood are rarely numerous. Occasionally, immature white cells have been absent from the blood as in the cases of Hewer (1937), Tudhope (1937), and Heller *et al.* (1947). Bleeding has occurred in several cases both with and without reported decreases in platelets (Hickling, 1937; Thompson and Illyne, 1940; Carpenter and Flory, 1941; and Heller *et al.*, 1947). Abnormal platelets, megakaryocytic fragments, and megakaryoblasts were observed by Hickling (1937), Carpenter and Flory (1941), Rosenthal and Erf (1943), and Heller *et al.* (1947). Other inconstant features such as increased fragility of the red cells, slight reticulocytosis, positive indirect van den Bergh reaction, and high blood uric acid levels have been occasionally reported.

In several cases the liver as well as the spleen has been the seat of a myeloid change—for example, McMichael and McNee (1936), Hickling (1937), and Stone and Woodman (1938). This has been found commonly in the dilated sinusoids, but also in the periportal areas or peripherally between adjacent lobules. Less frequently the lymph nodes have been involved as well, as reported by Stone and Woodman (1938), Vaughan and Harrison (1939), and Rosenthal and Erf (1943). Fibrosis of the spleen has also been described by Stone and Woodman (1938) and Jackson *et al.* (1940). Our Case 3 showed some fibrosis in the myeloid metaplasia of the spleen; the liver showed the metaplastic reaction mainly around the central vein.

The bone marrow has not been reported as myelosclerotic in all cases showing leuco-erythroblastic anaemia, splenomegaly, myeloid metaplasia, and symptoms of long duration. How far this may have been due to incomplete examination of the bones cannot now be decided. In nine cases of this syndrome called by them "agnogenic myeloid metaplasia" Jackson *et al.* (1940) described the bone marrow as myelosclerotic in six and hyperplastic, aplastic, and normal in the others. Similar variation is found in the literature, but most frequently the marrow is hypoplastic. Sometimes "hyperplastic foci of haematopoiesis" have been scattered through the fibrotic elements; in a few cases hyperplastic myeloid tissue and fibrosis have been recognized together.

In regard to the sequence of events in the marrow, Wyatt and Sommers (1950), analysing 30 cases, regarded the fundamental lesion as necrosis of partly matured erythroid and myeloid cells with hyperplasia of surviving, usually more immature, cells and marrow reticulum cells. Subsequently, foci of atrophy appear. Eventually "the marrow is relatively acellular, made up of scattered reticulum cells, between which is a pink fibrillar or granular matrix and with numerous dilated empty vessels surrounded by small groups of bizarre megakaryocytes or nondescript haematopoietic cells." The end stage in certain cases involves a distinct type of new bone formation with "focal granular deposits of calcium in the eosinophilic matrix" and later deposition of bone in a layer about part or all of the old trabecular surfaces. The bony radiographic appearances of myelosclerosis have been described by Sussman (1947) as initially widening and increased density of the trabeculae followed by deposition of bone in an irregular fashion throughout the marrow cavity without thickening of the cortices or periosteal reaction.

Nature and Pathogenesis

Most authors, with the notable exception of Heller *et al.* (1947), believe this syndrome to be a separate entity and not merely a variant of leukaemia. Carpenter and Flory (1941) listed the principal features which have been held to differentiate this syndrome from leukaemic myelosis (myelogenous leukaemia) as (1) the diversity of cell types in metaplastic zones in organs and in the bone marrow; (2) the commonly low white-cell count with the low proportion of circulating primitive cells; (3) the almost constant presence of nucleated red cells; (4) the frequency with which osteosclerosis and myelofibrosis are encountered; and (5) the absence of characteristic leukaemic infiltrations. Further differentiation from leukaemia has been made by Erf and Herbut (1944), who pointed out that "extramedullary haematopoiesis is a focus of normal bone marrow situated elsewhere than within bone and attempting to produce normal circulating red and white cells," whereas "leukaemic infiltration is a focus of infiltrating immature white blood cells which because of their inherent reproducing capacities produce more immature white cells." They have also drawn attention to the large numbers of giant cells in the metaplastic myeloid tissue in the organs. In view of its asso-

ciation at times with tuberculosis of the spleen (Swirtschewskaja, 1926), generalized infections (Brannan, 1927), and malignant metastatic deposits in the bone marrow (Hickling, 1937), it would appear that extramedullary haematopoiesis cannot be regarded simply as compensatory to the marrow sclerosis. Indeed, as Heller *et al.* (1947) have pointed out, more severe and persistent anaemias of other types do not occasion the massive extramedullary haematopoiesis found in myelosclerosis.

The myelosclerosis has been thought to result from an unknown toxin (Donhauser, 1908), the irritative effect of hyperplastic myeloid tissue (Hewer, 1937), or atrophy of the marrow (Wolf, 1932); it has been found in association with haemolytic anaemia (Wyatt and Sommers, 1950), metastatic carcinomatous deposits (Thompson and Illyne, 1940; Erf and Herbut, 1944), and tuberculosis (Hewer, 1937; Stone and Woodman, 1938). Windholz and Foster (1947) suggested the importance of Rh factor serological studies.

We agree with Vaughan and Harrison (1939) that the sclerosis of the marrow follows the same stimulus as produces extramedullary haemopoiesis. In other words the myelosclerosis is a dynamic process resulting from a definite stimulus rather than a sequel to atrophy of haemopoietic elements. The stimulus might be a deficiency in some nutritional factor, either direct or conditioned by other disease, or an abnormal metabolite. As pointed out by Vaughan and Harrison (1939) all the cell types involved in the hyperplasia are derived from a common source—the primitive reticulum-cell of Maximow. A common stimulus might therefore affect in degrees, varying from patient to patient, the osteoblasts, fibroblasts, the several series of haemopoietic cells, and megakaryocytes.

From this basic pathological process with diverse morphological possibilities a complex clinical and haematological syndrome results, not every case of which, as might be expected, will show all the various features recognized as characteristic. In this respect, Robson's case (personal communication, 1952) is of interest. Initially a sternal trephine was obtained showing marked osteosclerosis and megakaryocytosis with fibrosis, the blood picture being leuco-erythroblastic anaemia, and the spleen and liver showing myeloid metaplasia. Subsequently the blood count reached polycythaemic levels. Finally, at necropsy, three years after the onset, the marrow was seen to have reverted to a hyperplastic state with megakaryocytes still numerous, and some fibrosis still remaining but with little sign of the previous osteosclerosis, while the spleen and liver still showed metaplasia. In another case subsequent polycythaemia was described by McMichael and McNee (1936) 17 months after splenectomy had been undertaken for splenomegaly, myeloid metaplasia, and leuco-erythroblastic anaemia.

An indication of this diagnosis may be obtained during the investigation of obscure anaemia by the finding of difficulty in obtaining marrow from a sternal puncture and the absence of the characteristic "give" which occurs normally when the needle has penetrated to the marrow cavity. Most important, however, is the performance of marrow biopsy in cases showing features suggestive of the syndrome, or where sternal puncture fails.

Summary

Three cases of polycythaemia in two women aged 69 and 48 and a man aged 51, are described. Leuco-erythroblastic anaemia and myelosclerosis subsequently developed after 4, 12, and 5 years respectively.

Previous reports of leuco-erythroblastosis with myeloid metaplasia and myelosclerosis following polycythaemia vera are reviewed.

The syndrome, comprising leuco-erythroblastosis, myeloid metaplasia, and myelosclerosis, as revealed in the literature, has a varied clinical picture. It is thought to be distinct from myeloid leukaemia.

Vaughan and Harrison's view of the concomitant development from a common source—the primitive reticulum-cell of Maximow—of extramedullary haemopoieses and of myelosclerosis following some, as yet unknown, stimulus offers a reasonable explanation of the events.

We wish to thank Dr. L. Howells, Professor S. J. Hartfall, and Dr. J. R. H. Towers for permission to publish these cases, and Professor J. Gough and Dr. D. H. Collins for advice and criticism. We are grateful to Dr. D. H. Collins and Dr. T. W. Sutherland for haematological and pathological data in Cases 2 and 3.

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New regulations enable penicillin and aureomycin (the latter in a restricted form) to be used in the food of pigs and poultry, subject to certain safeguards. Both these preparations are controlled under the Penicillin Act, 1947, so that their retail distribution is otherwise limited to supplies given by, or under the direction of, doctors, dentists, and veterinary surgeons, or dispensed on their authority by pharmacists. The regulations have been made after consultation with the Medical Research Council and Agricultural Research Council, and come into operation on September 1. The antibiotics may be used either in the form of a supplement to be added to existing food or ready mixed with the food by the manufacturers of pig and poultry food. Safeguards to health are provided for in that (*a*) only minute quantities are needed and a maximum concentration is specified for both the supplement and the feeding-stuffs, and (*b*) the appropriate Health Minister must approve the composition of the diluent of the supplement. It will not be practicable to extract the antibiotic for use as medicine. These arrangements will not affect medical supplies. There is plenty of penicillin, and aureomycin will be used in the form of the residue from the process of extraction or in any other approved dilute preparation. The regulations also require certain information relating to the supplement and the antibiotic included to be given on the labels of the containers in such manner as the appropriate Agriculture Minister may require; they also empower him to require additional information to be given about the storage and use of supplement. The regulations apply to England and Wales, Scotland, and Northern Ireland, and are entitled the Therapeutic Substances (Supply of Antibiotics for Agricultural Purposes) Regulations, 1953.

SOME COMPLICATIONS OF TEMPORAL ARTERITIS

BY

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The first clear description of the condition known as temporal arteritis appeared in the article on intracranial aneurysm by Schmidt (1930); he did not, however, recognize the condition present. The disease was first fully described by Horton, Magath, and Brown (1932). Since that time many cases have been recorded, and it has become clear that the term temporal arteritis is an inadequate one, for the disease consists of a widespread arteritis affecting predominantly the branches of the external and internal carotid vessels (Bénard, Rambert, and Pestel, 1949), but in addition there has been evidence of arteritis elsewhere (Cooke, Cloake, Govan, and Colbeck, 1946; Cardell and Hanley, 1951).

Nothing is known of the fundamental aetiology of the disease; that it is allied to polyarteritis nodosa seems likely, but the changes in the affected vessels are not identical: the condition runs a more benign course and tends to affect very much older subjects than the latter condition.

The general course of the illness follows a fairly constant pattern. The subjects are usually elderly—average age 65 (Harrison, 1948)—and men and women are affected in approximately equal numbers. The onset is often insidious, with increasing malaise, mild fever, and pain in the head of variable intensity. When this pain is severe the slightest contact with the scalp at the site of pain may be unbearable, brushing or combing the hair may be very painful, and there may be pain on moving the jaw (Hoyt, Perera, and Kauvar, 1941; Bénard *et al.*, 1949).

In an uncomplicated case the pain and tenderness gradually subside, usually over a period of many weeks, and the general constitutional disturbance likewise resolves. In a high proportion of cases, however, other manifestations appear, and it is often these complications that cause the patient first to seek medical advice. Ocular complications are common. Wagener (1946) found visual disturbance in 18 of 37 patients; Bruce (1950) reported ocular involvement in 34 of 84 patients. Unilateral or bilateral blindness is common and is usually of sudden onset. Isolated sector defects may appear in the field of vision of one eye; there may be ocular palsy. Vertigo has been reported (Cooke *et al.*, 1946), there may be affection of the skin along the course of the temporal vessels, and small multiple ulcerative lesions of the nasal and buccal mucous membranes have been observed by Schweitzer and de Yong (1949).

Laboratory tests give variable results: there is a fairly constant rise in the erythrocyte sedimentation rate, there may be a slight polymorphonuclear leucocytosis, and an eosinophilia has been found by Hoyt *et al.* (1941).

Biopsy of a section of thrombosed temporal artery confirms the diagnosis. The affected vessel shows marked intimal thickening; infiltration of the media with lymphocytes, plasma cells, and at times giant cells; fragmentation of the elastic lamina of the media; and a thrombus in the lumen of the vessel in a varying state of organization and recanalization.

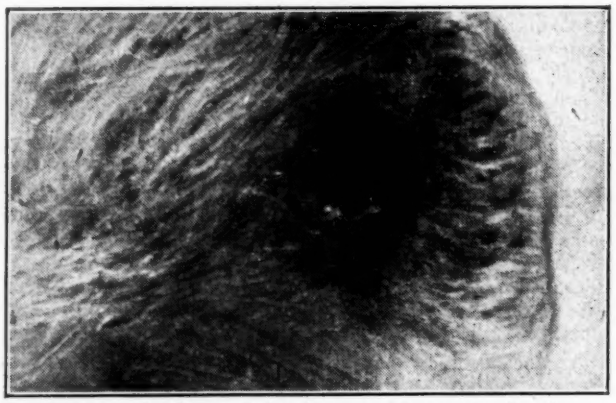
A description is here given of nine patients who suffered from temporal arteritis. It is of interest that all were country dwellers—an observation also made by Horton *et al.* (1932) and by Cohen and Harrison (1948).

Case 1

A woman aged 78, while recovering from a severe exacerbation of arthritis of the hips, wrists, and fingers in January, 1951, had intense temporal headache associated with intermittent fever to 102° F. (38.9° C.), a constant tachycardia of 100–120, anorexia, and loss of weight. The intensity of the pain increased, and the mere contact of any part of the head with the pillow became unbearable. Brushing the hair was impossible. She was at times mildly confused and delirious. Four weeks after the onset she awoke to find that vision was misty in each eye and within 48 hours all sight was lost. Examination at this time showed a considerable degree of emaciation. The whole scalp was acutely tender, and in all areas of the scalp thrombosed vessels could be felt. Both facial arteries were tender and non-pulsatile. Vision was lost in each eye; the pupils were of medium size and inactive to light. The optic disks were pale and the retinal arteries narrow and very tortuous. The peripheral vessels were sclerotic and the blood pressure was 150/70. There was widespread osteoarthritis, affecting the hands in particular.

One month later the pain and constitutional symptoms were subsiding. She had, however, developed an extensive area of necrosis of the scalp in the right parietal region near the vertex (see illustration). There was necrosis of the nasal septum, with a large perforation of the cartilage and offensive discharge.

The scalp healed very slowly over a period of four months, and the nasal discharge ceased. Nine months from the onset the patient was well although quite blind.



Photograph of Case 1 showing area of necrosis of scalp.

Comment.—The extent of the involvement of the scalp vessels seems to have been of a quite unusual severity—sufficient for a time to deprive one area of the scalp of an adequate blood supply.

Case 2

A woman aged 72 complained in July, 1948, of severe right-sided headaches and tenderness of the temporal region. Her past health had been good apart from severe arthritis of the spine and fingers. The onset of symptoms was gradual, with mild fever to 100° F. (37.8° C.) at times, and a tachycardia of about 120. When seen by me seven weeks from the onset she was pale, ill, and wasted. There was moderate tenderness of the right side of the scalp, the temporal vessels being hard, tender, tortuous, and non-pulsatile. The blood pressure was 220/120.

Salicylates gave some relief of pain, and the tenderness subsided in about one month. Three months later, while doing housework, she suddenly found that sight had failed

in the left eye. When seen one week later the left optic disk was pale, there was no perception of light, and the pupil did not react to direct illumination. The eye has since remained blind.

Comment.—The long interval between the onset of symptoms and the occurrence of blindness is by no means unusual. The part played by temporal arteritis may not at first be apparent if the symptoms have been slight.

Case 3

A man aged 66 was seen in August, 1949, complaining of intense left- and right-sided head pain of two week's duration, and giddiness and nausea of two days' duration. The onset of the latter symptoms had been sudden on rising in the morning. The giddiness was almost constant, with a feeling of being pulled to the left side, and was associated with a ringing tinnitus in the left ear.

Examination showed extensive thrombosis of the temporal vessels, mainly on the left side, with great tenderness. There was a coarse nystagmus to the left, and a moderate degree of nerve deafness on that side. The whole of the left side of the face did not move as well as the right. A blood count showed 26% of eosinophils in a total of 11,000 white corpuscles. The E.S.R. was 60 mm. in the first hour. A segment of the left temporal artery was removed under local analgesia with considerable resultant relief of pain. Section of the vessel showed typical changes of temporal arteritis.

The vertigo lasted about two weeks, at the end of which time there was considerable improvement. When he was seen six months later there was a mild degree of nerve deafness on the left side. There were no other symptoms.

Case 4

A man aged 78 was first seen in May, 1950, complaining of bitemporal pain and pain in the neck for two weeks, and loss of vision in the right eye for one week and in the left eye for two days. The onset had been gradual, with soreness in the temporal and occipital regions. After one week he noticed a dark patch in front of the right eye, and on waking next morning the eye was completely blind. Five days later he awoke to find the left eye blind. There had been no constitutional disturbance.

On examination the temporal and occipital vessels were tender and tortuous, but pulsatile. There was no perception of light in either eye, and the pupils were inactive. The right optic disk was pale. The blood pressure was 170/100. No other symptoms or signs developed, and he was well but blind five months later.

Case 5

A woman aged 69 started to complain in February, 1952, of severe pain on the right side of the head, pain on moving the jaw, and a recurrence of arthritis of the fingers, hips, and knees. Her symptoms gradually increased, and after four weeks she complained of double vision; this was followed by complete closure of the right eyelid.

On examination there was extensive bilateral thrombosis of the temporal vessels, the skin overlying the vessels was red and shiny, and the vessels were extremely tender. Tenderness was present over both temporo-mandibular joints. The temperature was 101° F. (38.3° C.) and pulse 110. There was much sweating. On the right side was a complete paralysis of the third cranial nerve. A blood count was normal, but the E.S.R. was raised to 40 mm. in the first hour.

Salicylates relieved the pain a little, and this subsided during the next six weeks. When seen in May, 1952, there was a partial right third-nerve paralysis, with dilated fixed pupil, incomplete ptosis, and defective adduction of the globe.

Case 6

A man aged 82 complained in March, 1952, of headache and soreness of the scalp which interfered with his sleep owing to the pressure of the pillow. There was, however, no major constitutional upset and he continued to lead an active life. Six weeks later, while weeding his garden, he noticed that the left eye was blurred, and very shortly afterwards the right eye was likewise affected. Within 24 hours all vision had been lost. When seen one week later there was bilateral optic atrophy with no perception of light. The pupils were large and inactive. The temporal vessels on both sides were thrombosed and tortuous, but were not tender. The blood pressure was 190/100. A blood film was normal. Two months later the patient was well but blind.

Case 7

A woman aged 73 was seen in May, 1952. Three months earlier she started to complain of "fibrositis" all over her head. After a week or two she noticed numerous tender "knobs" in the temporal regions and at the back of her head. The pain and tenderness persisted for about six weeks. Three weeks before attending hospital she noticed an appearance as if a spider's web were before the left eye; one week later, on waking, she could only see downwards and to the left with the left eye.

Examination showed numerous nodular thromboses in the temporal and occipital vessels, some of which were still somewhat tender. The left optic disk was pale. There was perception of hand movements with the left eye in the lower temporal field only. The left pupil reacted sluggishly to direct illumination. A blood count showed a mild normocytic anaemia with a leucocytosis of 11,500 per c.mm. The differential count was normal. The E.S.R. was 99 mm. in the first hour.

One month later her vision had improved to 6/60 with the left eye, and the density of the visual field disturbance was diminished.

Comment.—The incompleteness of the visual loss and its tendency to recover suggests, in the absence of obvious retinal change, that there was an incomplete or transitory occlusion of the central retinal artery.

Case 8

A man aged 72 developed in September, 1951, pain in the head of diffuse nature with malaise, anorexia, and slight fever. The pain increased in severity, and after two weeks he awoke to find that he was blind.

Examination showed tender thrombosed temporal vessels with some reddening of the overlying skin. There was no perception of light in either eye, and the pupils were dilated and fixed. The optic disks were normal. The blood pressure was 200/110. The constitutional and local symptoms subsided rapidly, leaving the patient permanently blind.

Case 9

This patient, a woman aged 78, was one of nine further patients suffering from temporal arteritis, in none of whom was there any central nervous complication. The history and findings in her case were typical of this group. She first complained of headache in the occipital and left temporal region in November, 1951. This symptom increased, and after 8 to 10 weeks there was complete loss of appetite. The pain was now severe and prevented sleep. A moderate bilateral conjunctivitis had developed. Her temperature was 100° F. (37.8° C.) and pulse 110. There was tenderness over the left temporal vessels, which were thrombosed and tortuous. Any contact or draught on the left side of the head was resented. The blood pressure was 220/120. A blood count showed: haemoglobin, 80%; white cells, 15,800 per c.mm. (87% polymorphs); E.S.R., 54 mm. in the first hour.

There was a quite rapid symptomatic and clinical improvement following the administration of mist. sod. salicyl. (*N.F.*). After four weeks the scalp tenderness was barely perceptible and appetite was returning. There was no fever.

Six weeks later her weight was increasing and pulsation could be felt in the previously occluded vessels.

Summary

The clinical course of nine patients suffering from temporal arteritis is described. The following points emerge: the patients are without exception elderly, often of arthritic disposition, and arteriosclerotic; the disease runs a protracted though benign course but may leave permanent damage to vision; temporal arteritis is a not uncommon cause of sudden visual failure in the elderly, and the underlying disease may be overlooked if the symptoms have not been severe or if they have occurred some weeks or months before; salicylates are of value, at least in the relief of symptoms. The ischaemia of the scalp may be sufficient to result in necrosis.

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DIETARY "FIBRE"* AND PREGNANCY TOXAEMIA†

BY

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Amongst the numerous hypotheses which have been put forward from time to time to account for the cause of pregnancy toxaemia is the "dietary" hypothesis. The most consistent advocates of this have been Theobald in the United Kingdom and Dieckmann in the United States.

Despite the fact that a consideration of the possible dietary factors has so far been unproductive of conclusions on the role of any one factor in the cause of the disease, the evidence indicates that a relationship of diet with toxaemia exists. The problem is to examine all the facts where the relationship seems to exist and try to fit them into a unified pattern.

A study of the literature reveals observations which apparently cannot be reconciled. For example, Ebbs, Tisdall, and Scott (1941) found that toxaemia and the incidence of stillbirth and neonatal deaths are more common in women with "poor" diets than in those with "good" diets or in those with poor diets supplemented throughout pregnancy with oranges, tomato pulp, wheat germ, milk, and vitamin D. How are these findings to be reconciled with the observation that toxaemia is very rare in some native populations living on so-called poor diets, and also with the findings that the incidence of eclampsia fell in Germany during the last two years of the 1914–18 war, and in the Netherlands during the 1939–45 war—that is, in periods of relative famine?

*The term "fibre" as used in this paper includes lignin, cellulose, and the hemicelluloses.

†Some of this work was carried out during the tenure of a World Health Organization Fellowship in 1952, but the statements made and the opinions expressed are not necessarily those of the Organization.

Diet and Toxaemia in Sydney

In a review of the monthly incidence of eclampsia in two hospitals in Sydney during the period 1938–45 I showed that eclampsia was more common from May to September (winter), when fruit and vegetables were scarce, than it was from November to March (summer) (Hipsley, 1949). In 1942, when there was a severe shortage of vegetables, the incidence of eclampsia was comparatively high, and the combined stillbirth and neonatal deaths reached record heights. The notion that this shortage may have contributed to the increased morbidity was strengthened by experience in New Guinea, where it was noted that native diets are predominantly vegetarian and that toxaemia is very rare. These observations suggested that there may have been a dietary factor which operated in the diet of peasant vegetarian communities and in the good diets of civilized communities but was apparently absent from poor diets of civilized communities.

Eclampsia in the Fiji Islands

In 1950 Bell and Wills noted a pronounced racial difference in the incidence of eclampsia between the indigenous Fijians and the Indians living in Fiji. In the three years 1947–9 there were 18 cases of eclampsia in 1,106 Indian confinements, while there were no cases in the same period in 717 confinements of Fijians. In 1949 there were 27 cases of pre-eclampsia in 416 Indian confinements, but no cases in 266 Fijian confinements.

The indigenous Fijians and the Indians living in the Fiji Islands are each a well-defined racial group differing widely in social, religious, and dietary habits. Such a situation seemed to offer a unique opportunity for the study of the dietary background of the disease. The staple food of the Fijian is a starchy fruit vegetable of which relatively large quantities are eaten, together with bananas, coconut, papaw, leafy greens, and small quantities of meat, fish, and crabs. The important foodstuffs in the Indian diet are flour (sharps), white rice, coconut oil, ghee, sugar, with small quantities of dhal, meat, milk, vegetables, and fruit. The bulk of this diet consists of the refined foodstuffs, white rice and flour (sharps).

A comparison of the diets of the two races shows that they differ greatly in "fibre" content (see Table I). This observation, together with the Sydney observations previ-

TABLE I.—*Fibre Content of Diets of Indians Living in Fiji Compared with New Guinea Diets*

Indian*				New Guinea†			
Foodstuff	g./Day /Head	Fibre‡ g./Day	Calories	Foodstuff	g./Day /Head	Fibre‡ g./Day	Calories
Bread	7·8	V.L.		Taro	106	1·80	
Sharps(flour)	317	V.L.		Sweet potato ..	170	1·70	
Rice, white	208·4	V.L.		Bananas ..	67	0·67	
Dhal ..	45 7	1·84		Yams	680	6·80	
Ghee ..	24·2	0		Pumpkin ..	17	0·17	
Coconut oil	35	0		Tapioca ..	17	0	
Potatoes ..	73·8	0·74		Brown rice ..	2·8	0·03	
Onions ..	3	0·06		Coconuts ..	39	1·24	
Sugar ..	54·9	0		Green leaves ..	2·8	0·45	
Milk ..	68	0		Papaw ..	28	0·28	
Vegetables and fruit	Small amount	V.L.		Fish	120	0	
Meat and fish ..	9·6	0					
Butter ..	3·7	0					
Total ..		>2·64	2,896	Total ..		13·14	1,600
		>0·9	1,000			8·2	1,000

* Bell and Wills, 1950.

† No quantitative assessment of Fijian diets is available. Quantitative data for Kavitaria (a village in the Trobriand Islands) have been used (see Report on the New Guinea Nutrition Survey Expedition, 1947. Department of Territories, Commonwealth of Australia, 1950.)

‡ The calculations for the fibre content of diets have been made using tables published by Nicholls (1951).

V.L.=Very little.

ously mentioned, suggested that further evidence be sought on whether a deficiency of dietary fibre could be concerned in the causation of toxaemia.

It was of interest to find out whether the incidence of eclampsia was high in the areas from which the Indians living in Fiji had emigrated—that is, Southern India—and whether the diets were similar. Mudaliar (1938) states that there were 148 cases of eclampsia in two years at his hospital in Madras; and Indian obstetricians who have worked in Southern India are unanimous in stating that eclampsia is very common there, and much more common in the cities than in the rural areas. Dr. Sunanda Bai (1952), an obstetrician who has worked in both the southern and the northern provinces of India, states that eclampsia is much less common in the northern provinces, especially in the Punjab, "where the diet is much better balanced and contains home-pounded wheat (instead of flour), more vegetables, more fruit, and more milk." Theobald (1946) has drawn attention to the very high incidence of eclampsia in the native population of Colombo (Ceylon), where the diet pattern is very similar to that of Southern India.

On the other hand, the diet pattern of the Fijians resembles closely that of the natives of New Guinea, amongst whom toxaemia is a rare disease.

Eclampsia and the Diet of Other Native Communities

Among the natives of the Transkei eclampsia is rare. The diet consists of meal porridge, milk, eggs, and a very small amount of meat (Crichton, 1947).

From reliable authorities, all of whom have had considerable experience in medical work in various native communities, information has been collected concerning the incidence of eclampsia and the diet pattern. Professor J. H. de Haas (1952), of Leyden, said that pregnancy toxaemia was very rare in Java. There the diet consisted of crudely milled and pounded rice, starchy root vegetables, some maize, and some leafy greens. Where fish was available this was eaten. Pregnancy toxaemia was very uncommon in the Celebes according to Dr. de Wijn (1952), of Leyden. The diet consisted mainly of home-pounded rice, leafy greens, coconut, and only a small quantity of starchy root vegetables, melons, and fruit. On the coast some fish was eaten. It is noteworthy that in these communities, where toxaemia was uncommon, the diet was comparatively rich in fibre.

Trends in Eclampsia in War-stricken Countries

One of the most notable features of eclampsia is that the incidence has been observed to vary in the same geographical area, apparently as a result of a marked change in the environment. Thus a change in eclampsia incidence has been particularly noticeable in war-stricken countries. The effect of war has been by no means consistent: apparently it has sometimes been adverse and at other times beneficial.

Hong Kong.—King and Ride (1945) reported that in Hong Kong in 1940–1 there was a striking increase in the incidence of eclampsia, reaching almost epidemic proportions. This coincided with a serious outbreak of beriberi. Eclampsia

TABLE II.—*Showing Correlation of Fibre Content of Diet with Incidence of Eclampsia or Pregnancy Toxaemia*

Group	Description of Diet	Dietary Fibre Grading*	Eclampsia† or Toxaemia	Authority
New Guinea natives Fijians	Starchy roots, green leaves, nuts, fruit, plus small amounts of fish and meat	++++	0	Hipsley (1949); Bell and Wills (1950)
Punjab	Home-pounded wheat, starchy roots, pumpkin, fruit, plus a little milk	++++	+	Bai (1952)
Transkei (South Africa)	Meal porridge, milk, eggs, and small amount of meat	++++	0	Crichton (1947)
Java	Home-pounded rice, green leaves, maize, starchy roots, little fish	++++	+	de Haas (1952)
Celebes	Home-pounded rice, greens, coconut. Small amounts of vegetables, melons, and fruit	++++	+	de Wijn (1952)
Indians (Fiji)	Polished rice, flour (sharps), ghee, coconut oil, dhal. Small amounts sugar, meat, and vegetables	+	++++	Bell and Wills (1950)
Indians (South India)	Ditto	+	++++	Mudaliar (1938); Bai (1952)
Colombo	Ditto	+	++++	Theobald (1946)
Europeans (Toronto) "poor" diet group	Inexpensive high-energy-yielding foods. Minimum of "protective" fruit and vegetables which are more costly	Increased	Reduced	Ebbs, Tisdall, and Scott (1941)
Europeans (Toronto) "good" diet group	Increased consumption of fruit and vegetables	↓	↓	Ebbs, Tisdall, and Scott (1941)

TABLE III.—*Showing the Apparent Effect of a Change in Fibre Content of the Diet on the Incidence of Eclampsia or Toxaemia*

Group	Period of Change	Dietary Change	Dietary Fibre Grading*	Eclampsia† or Toxaemia	Authority
Hong Kong	1939	Mixed diet	+++	++	King and Ride (1945)
	1940–1	To polished rice	+	+++	King (1947)
	1945	To mixed diet	+++	++	
Netherlands	1940	Mixed diet (70% extra bread)	++	Reduced	Holmer (1947)
	1944	To food shortage (90% extra bread) and starchy roots and vegetables	++++	↓	Duncan *et al.* (1952)
	1945	To relief of famine, refined high-calorie foods (70% extra bread)	++	Increased ↓	
Scotland	1939	Mixed diet containing 70% extra bread	++	Reduced	Baird (1952)
	1942 *et seq.*	To 85% extraction bread and more vegetables	+++	↓	
Sydney	1939	Mixed diet	+++	+	Hipsley (1949)
	1942	To acute shortage of vegetables	++	++	
	1943	To normal mixed diet	+++	+	
"	Summer	Mixed diet containing moderate fruit and vegetables	+++	Increased	Hipsley (1949)
	Winter	To reduced consumption of fruit and vegetables	++	↓	
"	Control of weight gain in pregnancy	Restriction of concentrated high-energy foods	++	++	Hamlin (1952)
		With increased consumption of fruit and vegetables	+++	0	

* Fibre grading (approximate): ++++ Very high = above 4 g./1,000 cals. +++ High = 2–4 g./1,000 cals. ++ Moderate = 1–2 g./1,000 cals. + Low = below 1 g./1,000 cals.

† Incidence of eclampsia (approximate): ++++ Very high = 8 eclamptics/1,000 deliveries. +++ High = 2–8 eclamptics/1,000 deliveries. ++ Moderate = 1–2 eclamptics/1,000 deliveries. + Low = below 1 eclamptic/1,000 deliveries. 0 Absent or very low.

was particularly common in the beriberi cases, and Browne (1944) has commented that the data of King and Ride show that eclampsia was 50 times more common in women with beriberi than in those without it. On the other hand, vitamin B_1 has proved valueless either in the prevention or in the treatment of the disease. It is of interest to examine the changes in diet which resulted in this increase of beriberi. King and Ride state that there was a change from a relatively mixed diet to one of polished rice, owing to an influx of refugeees from war areas, with consequent poverty and overcrowding of the city. After the war the eclampsia had declined to the original 1938 level, and the beriberi incidence had declined also (King, 1947). Burgess (1952) has pointed out that since the war less white rice has been available in Hong Kong. The change in the fibre content of the diets of Hong Kong would seem to run parallel with the change in the incidence of eclampsia.

Netherlands.—Contrary to experience in Hong Kong, the impact of war apparently had a beneficial effect on the incidence of eclampsia. Holmer (1947) and Duncan, Baird, and Thomson (1952), the latter using data supplied by Posthuma and others, have reported that the incidence of toxaemia fell in the Netherlands from 1940 to 1945, but rose again after the war to almost its pre-war level. Holmer states that in Holland during the food shortages pregnant women did remarkably well. There were few cases of eclampsia, but immediately after the relief of the famine he saw seven cases, three of which were fatal. The first food distributed to the starved population had a high calorific value, and consisted mainly of fats, protein, and sugar; it was also very salty. During the war the diet pattern in the Netherlands altered as food became scarcer. Bread, which before the war was made from 70% extraction flour, was made from flour which at times was 90–95% extraction; turnips and potatoes became much more prominent in the diet; and in 1944, during the worst period of famine, even linseed meal, tulip bulbs, and sugar beets were eaten. There is no doubt that the fibre content of the diet increased from 1940 to 1944 and has decreased again since that date.

Scotland.—Duncan, Baird, and Thomson (1952) have shown that in Scotland from 1943 onwards a steady and considerable fall occurred in the stillbirth rates resulting from toxaemia. This fall they attributed to "improvement from 1941 onwards in the efficiency of the physiological mechanisms which govern the growth and vitality of the foetus." They thought the improvement was unlikely to have been due to better antenatal care, but was probably due to improved economic conditions, assisted by the effects of scientific rationing. An important widespread change in the diet was the change from 72% extraction bread to 85% early in 1942. The fibre content of 70% extraction flour is negligible, while that of 85% extraction is 1%. This single change in bread, a staple foodstuff, would have brought about a widespread increase in the fibre content of the diet from approximately 1.2 g. per 1,000 calories to 2.4 g.

Effect of Control of Weight Gain in Pregnancy

Hamlin (1952) published the results of a three-year attack on eclampsia at the Crown Street Women's Hospital in Sydney. He claims that eclampsia has virtually been eliminated by changing the diet from a "high-carbohydrate, low-protein diet to a low-carbohydrate, high-protein, high-vitamin diet before mid-pregnancy." These measures were coupled with increased antenatal supervision and control of excessive weight gain in mid-pregnancy by dieting. The dietary changes advocated by Hamlin would have the effect of increasing the intake of fibre. Especially is this so in the case of diets designed to limit weight gain in pregnancy, where the restriction of the concentrated high-calorie foods such as flour, sugar, and fats is countered by an increased intake of the more bulky but less fattening fruits and vegetables.

In assessing Hamlin's results it should be noted that eclampsia—that is, the actual occurrence of fits—can often be prevented by careful supervision and treatment of toxaemia patients. In other words, the incidence of *eclampsia* is susceptible to antenatal care, and does not always bear a true relationship to the incidence of *toxaemia*, especially where there is a high standard of obstetric service. Baird (1952) is of the opinion that the combined stillbirth and neonatal death rate has a much closer relationship with the true toxaemia incidence, because these morbid conditions are so often the result of toxaemia. Unfortunately Hamlin does not give evidence on the incidence of toxaemia (without eclampsia) or on the combined stillbirth and neonatal death rates.

Toxaemia in Poor and Good Diets of Urban Communities

One of the characteristic features of poor urban diets is that people tend to satisfy hunger with concentrated energy-producing foods which are cheap, whilst neglecting the more costly "protective" foods, such as fruit and vegetables. These foods, in addition to being rich in minerals and vitamins, also contain fibre. Ebbs, Tisdall, and Scott (1941) demonstrated that good diets and poor diets, supplemented with a number of fruits and vegetables (see above), apparently had a beneficial effect on the incidence of toxaemia. These diets undoubtedly had a higher fibre content than the poor diets.

In review, most of the above observations relating diet to the incidence of pregnancy show that toxaemia is more common where the fibre content of the diet is low. The evidence for this is summarized in Tables II and III.

Summary

The incidence of pregnancy toxaemia in various groups of people consuming widely different diets, together with observations of trends in the incidence of this disease in the same group of people but at different periods (such as during wartime), has been discussed.

The suggestion is made that some factor or factors associated with the "fibre" content of the diet tend to inhibit the occurrence of toxaemia.

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From the *Gentlemen's Magazine*, August, 1853: "The Royal Family has been suffering from measles. It first appeared on H.R.H. the Prince of Wales, who in consequence was absent from his brother's [Prince Leopold's] christening. On July 8 it was announced that Prince Albert [Prince Consort] was attacked, and on the 19th that Her Majesty also had the complaint. Meanwhile all the royal children except the first have successively taken the infection. The whole Royal Family have passed through the disease very favourably. On July 6 the foundation stone of the Medical Benevolent College was laid in Epsom . . . H.R.H. Prince Albert, who had promised to lay the stone, was absent from illness."

PROSTATIC DYSPEPSIA

BY

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Although "silent prostatism" is a well-recognized clinical condition, it is surprising how few references to it occur in the current literature, and, with one or two possible exceptions, mention of the condition is conspicuous by its absence from the standard undergraduate and postgraduate textbooks of surgery and urology. Ewert and Summons (1951) have drawn attention to the not uncommon insidious onset of prostatic obstruction. They have emphasized that this condition may present itself with symptoms unrelated to the genito-urinary tract, and state that these symptoms are due to varying degrees of renal insufficiency.

Silent prostatism is more common than is generally realized and may present as a gastro-intestinal disturbance, with a history suggestive of carcinoma of the stomach or early hepatic cirrhosis in the absence of urinary symptoms and before there is biochemical evidence of renal insufficiency or azotaemia. Eighteen cases of this type were encountered during the last five years in a series of just over 200 patients who had undergone prostatectomy.

The presenting symptoms of this syndrome, which may well be called "prostatic dyspepsia," are upper abdominal discomfort or pain, nausea, and anorexia. Urinary symptoms are absent, but the residual urine is invariably much increased and the cystoscopic appearances confirm the diagnosis. The following case histories are typical.

Three Case Reports

Case 1.—A man aged 73 was admitted to a medical ward for investigation. He had a four-months history of dyspepsia, anorexia, and vomiting with loss of weight. Barium meal examination and fractional test meal and liver-function tests showed nothing abnormal. Blood urea was 27 mg. per 100 ml. An intravenous pyelogram showed normal function of both kidneys, but a large filling defect at the base of the bladder and considerable vesical retention in the post-micturition film. Cystoscopy was attempted, but the instrument was not long enough to get through the prostate, which could be felt above the symphysis pubis when the bladder was empty. A one-stage prostatectomy was carried out and a gland weighing 340 g. was removed. Three months after operation the patient declared himself to be in perfect health with complete restoration of his digestive powers.

Case 2.—This patient, aged 65, was referred by his general practitioner with a history of four months' anorexia, pain, and nausea. He had lost 2 stone (12.7 kg.) in weight. He would admit to no urinary symptoms. Barium meal, test meal, and liver-function tests revealed no abnormality. Blood urea was 34 mg. per 100 ml.; haemoglobin, 76%. The history was so typical of gastric carcinoma that laparotomy was advised. This was performed, but no lesion of the stomach or intestines was detected. When the hand was palpating the pelvis the bladder was felt to contain several ounces of urine. Subsequent investigations showed a residual urine of 8 oz. (230 ml.), a normal intravenous pyelogram, and a moderately trabeculated bladder. The man did not rise at night to pass his water and had complete control with no delay or urgency. Removal of a small prostate (24 g.) cured his digestive symptoms, and his weight was back to normal three months after operation.

Case 3.—A man aged 68 attended his doctor complaining of feeling out of sorts with loss of appetite and constipation. He had no urinary symptoms, sometimes rose once at night to micturate, but passed urine with a good stream. On examination he had a bladder palpable 3 in. (7.5 cm.) above the symphysis pubis. The prostate was moderately enlarged but benign. The blood urea was 36 mg. per 100 ml., and the urine was uninfected. An intravenous pyelogram showed normal concentration in the kidneys with no hydronephrosis. The bladder shadow was enlarged. Cystoscopy showed moderate intravesical projection of the prostate and trabeculation of the bladder, with 30 oz. (850 ml.) residual urine. This examination precipitated an acute retention of urine, so a closed transvesical prostatectomy was performed 24 hours later. Convalescence was delayed by a femoral thrombosis, but when seen three months after operation, although he still had a little swelling of the leg, he said he was feeling fitter than for some time.

Remainder of Series

Fifteen other cases of the condition have been seen, a summary of whose clinical histories are tabulated below.

Details of Cases

Age	Predominant Symptom	Initial Provisional Diagnosis	Blood Urea mg./100 ml.	Urine	Residual Urine	
					oz.	ml.
74	Anorexia	Carcinoma of stomach	34	Sterile	8	230
72	Epigastric discomfort	,, ,,	39	,,	6	170
58	,, ,,	,, ,,	31	,,	14	400
60	Nausea	Gastric ulcer	44	Infected	6	170
64	Epigastric discomfort	Duodenal ulcer	32	Sterile	18	510
70	Anorexia	Cirrhosis	37	,,	6	170
78	Nausea	,,	40	,,	14	400
61	Anorexia	Carcinoma of stomach	28	,,	20	570
74	Nausea	Gastric ulcer	31	Infected	8	230
72	Epigastric discomfort	,, ,,	42	Sterile	23	655
82	,, ,,	Duodenal ulcer	36	,,	8	230
76	Nausea	Carcinoma of stomach	45	,,	6	170
72	Epigastric discomfort	Gastric ulcer	29	,,	15	425
70	Anorexia	Carcinoma of stomach	31	,,	10	285
54	,,	Cirrhosis	38	,,	22	625

Comment

It is a well-recognized fact that patients who have had a prostatectomy frequently volunteer the information after the operation that they feel fitter than they have felt for some time. The observation is not limited to those in whom there has been some degree of uraemia.

Several of the patients in this series were submitted to detailed investigations, including urea concentration and clearance tests, blood alkali reserve, etc., and in none has there been evidence of renal impairment.

The cause of the syndrome of dyspepsia, nausea, and anorexia, associated with prostatic obstruction which has not gone on to the stage of renal impairment, is not clear, but is in my submission a definite entity which is not generally recognized until uraemic symptoms supervene. It would seem that the importance of these cases, which in my experience account for a little over 5% of all patients requiring prostatectomy, lies in the fact that, unless the clinician concerned, usually not a surgeon or urologist, is alive to the possibilities of prostatic obstruction being the underlying cause, the patient may be sent away after a negative gastro-enterological examination or submitted to an unnecessary laparotomy, when the catheter to measure the residual urine or the cystoscope will make the diagnosis clear.

Summary

A syndrome of epigastric pain, nausea, and anorexia is a not uncommon initial complaint in patients with prostatic obstruction without urinary symptoms.

A series of eighteen patients are described with this syndrome in whom there was no real evidence of renal impairment.

The importance of the condition lies in the fact that after a negative gastro-enterological investigation it can be, and often is, overlooked until uraemic symptoms supervene.

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HYPERPARATHYROIDISM WITH NORMAL SERUM CALCIUM

BY

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Osteitis fibrosa cystica was first described by von Recklinghausen in 1891, but the first clear demonstration that a parathyroid adenoma was the cause came in 1925, when Mandl cured a man crippled with the disease by the removal of such a tumour. Since then our knowledge of the disease, its clinical, radiographic, and biochemical features, has steadily increased, though as recently as 1950 Rienhoff estimated that there were only 597 proved cases in the world's literature or known to him personally. Thus the disease is rare enough to warrant a record of every case, especially when there are any unusual findings, and since treatment is so effective.

Case Report

A spinster tea-packer aged 33 first consulted her doctor in February, 1951, because of "rheumatism" in the legs and back for five months. Before this her health had been good; she had lived an active life and had played tennis during the previous summer. The aching pain had started in her right thigh rather suddenly in September, 1950, and had spread in several weeks to involve the lower back, thighs, and knees. The pain was made worse by movement, but did not prevent sleep. She noticed increasing weakness in the legs, so that walking, especially starting off, became difficult: a waddling gait developed. These disabilities caused her to stop her work at Christmas, 1950. The symptoms became increasingly severe; some aching and weakness developed in the right shoulder, and a painful lump appeared below the manubrium sterni. She had noticed some frequency of micturition, which disturbed her twice each night.

She was referred to the medical out-patient department, where the most striking abnormality was her gait as she entered the room. It resembled the waddling of a duck, and was thought to be due to muscular weakness, especially of the hip abductors. She was of stocky build, and had a marked thoracic kyphosis, which, though present since childhood, she thought had become more pronounced. The bones were not tender, and passive movement of the limbs was full and pain-free. There was definite muscular weakness of the abductors, flexors, and extensors of the hip-joints, but no wasting and no reflex or sensory changes. Examination of the neck, lungs, heart, and abdomen was normal. The blood pressure was 130/90 and weight 8 st. 9 lb. (54.9 kg.). There was a tender bony lump in the sternum between the third costal cartilages. *X*-ray examination of the pelvis revealed a generalized osteoporosis, so she was admitted for investigation with a tentative diagnosis of hyperparathyroidism.

Investigations.—In order to confirm the clinical diagnosis and to exclude in particular multiple myelomatosis and polyostotic fibrous dysplasia (Albright's disease) extensive investigations were made. Skeletal *x*-ray films revealed generalized osteoporosis, with a "moth-eaten" appearance in the skull (Fig. 1), and early fibrocystic areas, especially in the pelvis and right upper humerus. There was a fracture of the body of the sternum, and a loss of the lamina dura of the teeth. No calcification was seen in the renal tract. Four pre-operative serum calcium estimations (10.8, 10.32, 9.8, and 9.7 mg. per 100 ml.) during three months were within the normal range: the method used was that described by Trevan and Bainbridge (1926). Two out of the three plasma phosphorus estimations (1.7, 2.2, and 1.8 mg. per 100 ml.) were, however, below normal limits. The serum alkaline phosphatase was 92.4, 94.4, and 98.0 King-Armstrong units per 100 ml. at monthly intervals. The blood urea (34 mg. per 100 ml.) and urea clearance were normal, as were the serum proteins (total, 6.7 g.; albumin, 4.16 g. per 100 ml.). An eight-day calcium balance showed that on an intake of 97 mg. daily her average urinary excretion was 322 mg. and faecal excretion 162 mg., a daily negative balance of 387 mg. The combination of low plasma phosphorus and a negative calcium balance, even in the presence of normal serum calcium, made the diagnosis almost certain.

A sternal bone biopsy showed osteoclastic destruction of bone trabeculae associated with proliferation of fibrous tissue. There was very little evidence of new bone formation and there was no mosaic pattern in the islets. The appearances were those of osteitis fibrosa cystica.

A blood count showed: red cells, 4,300,000 per c.mm.; Hb, 11.9 g. (80%); colour index, 0.9; E.S.R. 4 mm. (Wintrobe corrected); white-cell count, normal. There were no casts, cells, or albumin in the urine.

Operation.—On June 11, 1951, Mr. E. G. Muir explored the neck through the usual collar incision. A normal parathyroid gland was identified on the left side, but a small parathyroid adenoma was found attached to the right lower pole of the thyroid. It was removed by dividing the short pedicle. The adenoma was deep red in colour with a smooth surface; it measured 1.8 by 1 by 0.8 cm. and weighed 0.9 g. Microscopical examination showed parathyroid tissue composed almost entirely of "wasserhelle" cells.

Subsequent Course.—The patient was given 2 pints (1,140 ml.) of milk, 60 gr. (4 g.) of calcium lactate, and 10,000 units of calciferol daily from three days before operation until six months afterwards. The bone pain vanished immediately after operation, and muscle strength returned within a few weeks. Five days after operation latent tetany was detected by a positive Chvostek's sign; at that time the serum calcium was 7.9 mg. per 100 ml. The dose of calcium lactate was increased to 240 gr.

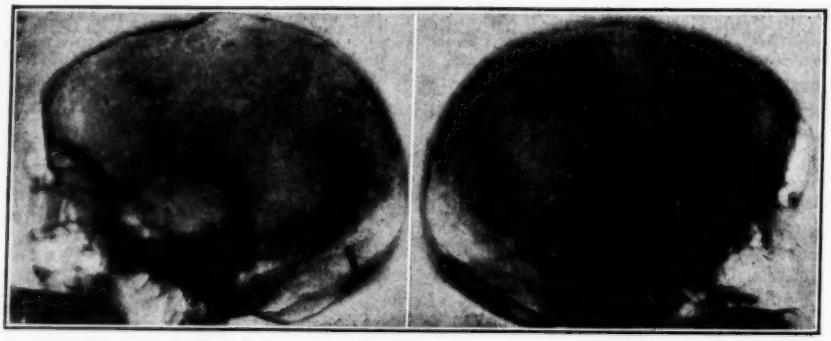

FIG. 1 FIG. 2

FIG. 1.—Skull. Moth-eaten osteoporosis. FIG. 2.—Skull. Six months after operation.

(16 g.) daily. The sign disappeared after two days, and thereafter convalescence was uneventful. Subsequent biochemical tests are recorded in Fig. 3. On the sixteenth day the daily urinary excretion of calcium had fallen to 40 mg. despite an intake of more than 3,900 mg. of calcium ion. Three months after operation radiographs of the bones showed much recalcification; the gait was normal and the patient symptom-free. Six months after operation radiographs were almost normal (Fig. 2), and the phosphatase had fallen to 14.7 units per 100 ml. All treatment was then stopped.

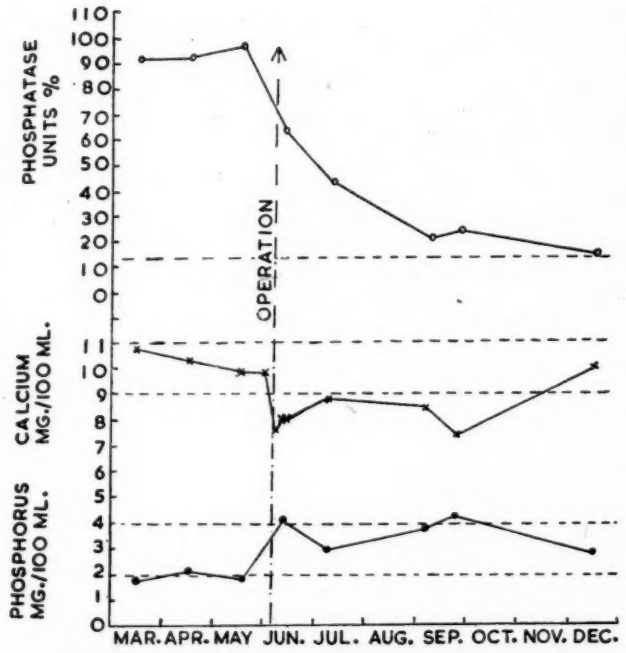

FIG. 3.—Serial estimations of serum alkaline phosphatase, serum calcium, and plasma phosphorus. Normal ranges are shown thus - - - - - -.

Discussion

This case is of special interest because of the very short duration of symptoms, the normal serum calcium, and the rapid and complete response to treatment. Most reported cases have had symptoms for more than two years before the diagnosis has been made (Norris, 1947). The importance of early diagnosis is seen in Rienhoff's own 27 patients, who were followed for several years: within a few years of operation 10 died from uraemia or hypertension following nephrocalcinosis. In general, the fatalities were among those with the longest histories before operation and those with renal damage.

Since the prognosis is so much improved by early diagnosis, the early symptoms of hyperparathyroidism merit emphasis. They are usually described as: (1) due to decalcification of the skeleton—aching bones, deformities, spontaneous fractures; (2) due to hypercalciuria—polyuria, thirst, renal pain; or (3) due to hypercalcaemia—anorexia, nausea, constipation, muscular weakness, increasing muscular fatigue, waddling gait.

Although this patient had the symptoms usually ascribed to hypercalcaemia, her serum calcium was in fact within normal limits. Four estimations were made in three months, by an experienced technician, at a time when the patient had marked symptoms from the disease. It is obvious that these symptoms may be caused by factors other than hypercalcaemia.

Gutman and his colleagues (1936), reviewing the serum calcium levels of 114 cases of hyperparathyroidism, found values below 11 mg. in five only and below 12 mg. in 23 only. They thought that normal serum calcium values could be explained in one of four different ways.

1. *Renal Failure.*—This commonly occurs in cases of long duration. It causes phosphate retention with secondary depression of the serum calcium level. This is well illustrated by Case 2 of Gutman *et al.*, in which renal failure occurred while the patient was in hospital, with a fall in calcium from 12.4 to 10.5 mg. along with a rise in phosphorus from 3.9 to 6.1 mg.

2. *Hypoproteinaemia.*—Normally about 50% of the total serum calcium is bound to protein; the remainder is ionic calcium, and it is this fraction which is raised in hyperparathyroidism. Coincidental hypoproteinaemia, with a low protein-bound fraction, may thus mask a pathologically high ionized calcium when the total serum calcium is normal.

3. *Insufficient Testing.*—Sometimes a normal value is found in an isolated test, but repeated estimations show the typical elevation. For instance, the initial estimation of Case 2 of Albright *et al.* (1934) showed a level of 10.4 mg.; on subsequent testing it was 12.3 mg.

4. *Short Duration of Symptoms, with Normal Kidneys.*—Under these circumstances the excess calcium mobilized from the bones can be excreted without accumulation in the blood: such is the explanation in the present case. The kidney-function tests were normal, as were the serum proteins; the disease was active as judged by the bone pain and negative calcium balance, yet the serum calcium was normal on four occasions during three months.

Summary

An example of hyperparathyroidism is described in which the duration of bone pain and weakness was only five months and the serum calcium was normal. The early symptoms of the disease are reviewed and emphasized. The normal serum calcium was thought to be due to effective excretion of calcium by the kidneys. A parathyroid adenoma was removed successfully and the patient's health restored.

I wish to thank Dr. Clifford Hoyle, under whose care the patient was admitted, for help with this paper; Mr. E. G. Muir, who did the operation; Dr. A. M. Rackow for the radiographs; Professor C. H. Gray for the biochemical investigations; and Dr. B. S. Cardell for the histology.

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The outstanding social problem of our age, particularly in northern towns, is unsatisfactory housing, says Dr. C. Metcalfe Brown, medical officer of health to the city of Manchester, in his annual report. "Notwithstanding the strenuous efforts of the housing department in providing new houses," he writes, "the housing position in the city is bad. Hundreds of cases annually seek the help of the health department for the alleviation of hardship caused by wretched housing conditions. The department takes all action within its power, but this action is severely limited by the controlling factor—namely, the grave shortage of new houses. Enormous distress is being caused to thousands of Manchester people because of the inadequacy of housing accommodation. The health, happiness, and integrity of family life cannot be achieved and maintained to the full unless housing is good."

TREATMENT OF LIME BURNS OF THE EYE WITH CORVASYMTON AND UNDERMINING OF CONJUNCTIVA

BY

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The satisfactory results of the treatment of chemical burns of the eye with "corvasymton" as reported by Fischer, Hodgson, and Wagenaar (1950) and Wagenaar (1952) drew my attention to this new preparation. Its use started quite accidentally when in a carbide burn of the eye it was instilled by mistake instead of vitamin A oil. The cornea was clear and transparent after instillation every 15 minutes for three hours. A generous supply of corvasymton enabled me to carry out an intensive treatment of several cases of lime burns of the eye. Here is a record of some of them.

Case 1

On June 24, 1952, a 23-year-old man was hit on the right eye by a handful of quicklime thrown at him by a fellow workman. When at last the eye was cleansed of all particles of lime, by means of copious irrigations with saline solutions and by pledgets of cotton-wool carried on a conjunctival forceps, the lower third of the cornea presented a porcelain-white appearance. The remaining part of the cornea was so hazy that the iris could scarcely be seen. The conjunctiva of the entire lower fornix was greyish white in colour, and showed such a severe degree of chemosis that no blood vessels could be seen. Vision was reduced down to vague hand movements.

The eye was immediately operated upon. The "necrotic" conjunctiva was loosened up by means of a straight keratome along the limbus corneae in a sector between 5 and 7 o'clock and extensively undermined in a peripheral direction down to the fornix. The conjunctiva was cut at the limits of the undermined area so that a trapdoor flap with the hinge at the fornix was formed. A portion of the sclera was laid bare. No part of the conjunctiva or subconjunctival tissue was removed. There was no loss of blood. This fact suggests that there was occlusion of the blood vessels. The eye was irrigated with corvasympton 10% and instillation continued every hour.

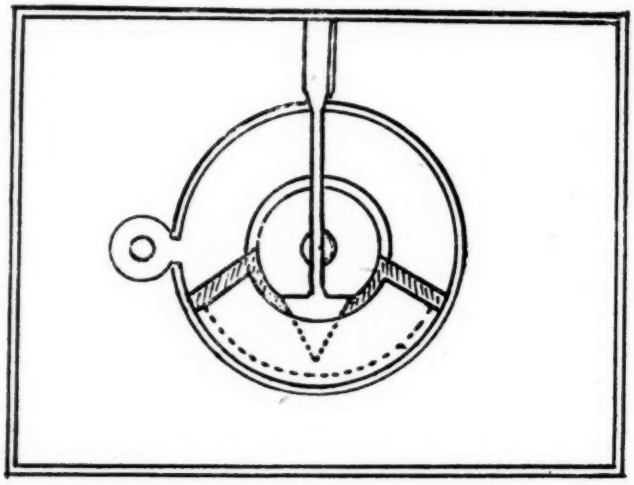
The chemosis soon started to subside and the conjunctiva regained very gradually its normal pink colour. The cornea took a longer time to acquire its bright healthy appearance. The cloudiness of the upper part of the cornea was the first to disappear, and, except for one tiny spot at 6 o'clock near the limbus, the porcelain-white patch cleared off completely. There remained, however, a small narrow symblepharon deep down in the lower fornix in the same line as the spot on the cornea; it never showed any sign of increasing in extent, and no further intervention was necessary.

Vision in both eyes was 6/12 unaided and 6/6 with glasses. There was never any sign of a rise of intraocular tension and there were no corneal vascular changes. Atropine was never used. The patient was discharged three weeks after admission. I think that, had I loosened up the conjunctiva at the limbus along a wider section, both the corneal opacity and symblepharon would have been prevented.

Case 2

On July 17, 1952, a 17-year-old youth was admitted into hospital for a lime burn of the right eye. On examination the cornea and conjunctiva presented much the same degree of injury as Case 1. No blood vessels were to be seen on the chemotic conjunctiva of the lower fornix. There was a porcelain-white patch on the lower part of the cornea. Diffuse cloudiness of the cornea was very marked. Vision was limited to hand movements.

As there was a considerable degree of blepharospasm, the patient was operated on under general anaesthesia. All residual particles of lime were removed. The same procedure was followed as in Case 1. However, in an attempt to prevent all possible complications, I loosened up the ocular conjunctiva on a much wider section—that is, between 3 and 9 o'clock (see Fig.). The eye was then irrigated with corvasymton solution and instillation continued hourly.



The chemosis gradually disappeared and the conjunctiva soon began to show its normal appearance. The conjunctival flap was noticed to gain reattachment to its scleral bed. The cloudiness of the cornea gradually disappeared. After one week the patient started to complain of pain in the eye. Instillation of fluorescein solution revealed a fairly large staining spot in the cornea near the limbus at 6 o'clock. The eye was kept bandaged between the instillations. After five days there was no sign of corneal staining.

When discharged after three weeks the cornea was clear and the lower fornix was completely free. No corneal vascularization was present. One month after being discharged the vision in both eyes was 6/6.

Case 3

A boy aged 8 was struck in the left eye by a piece of quicklime. The injury was localized mainly to the upper fornix region. The cornea was diffusely hazy and he could count fingers at one metre. Instillation of corvasymton every hour was immediately started. As the chemosis was not pronounced, no undermining of conjunctiva was performed. Three days later it was noticed that the conjunctiva in the inner angle of the upper fornix was very swollen. The patient was examined under general anaesthesia. A piece of lime had burnt its way deep into the conjunctiva, which was loosened up throughout the upper half of the limbus and deeply undermined peripherally. The piece of lime along with the conjunctiva was excised.

Recovery was quick and complete. When the patient was discharged two weeks later there was a small adhesion deep into the inner angle of the superior fornix corresponding to the excised parties of the conjunctiva. The cornea was completely free from opacities. Vision was 6/6.

Case 4

A man aged 35 was injured in both eyes by a splash of quicklime. The burn was mainly limited to the corneae, which were very hazy. There was a moderate degree of swelling of the ocular conjunctiva. Vision was reduced to counting fingers at one metre. Corvasymton was instilled every hour. No undermining was done. The corneae gradually acquired their normal brightness and the patient was discharged after 10 days.

Case 5

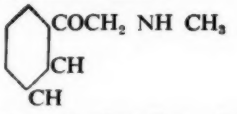
On September 8, 1952, a man aged 70 was admitted to hospital for a lime burn of the right eye. On examination the cornea was very hazy and vision was reduced to hand movements. The ocular conjunctiva was moderately swollen. The haziness of the cornea disappeared after two weeks. But there was a tiny persistent staining spot at 7 o'clock just within the limbus. When the patient was discharged after six weeks the cornea was clear except for a small dense opacity corresponding to the staining spot. The fornix was free.

Discussion

Corvasymton is an oxyphenyl-methylaminoethanol tartrate solution. It is related to "sympatol," which is closely allied to adrenaline: dioxyphenylmethylaminethanol. When corvasympton solution 10% is instilled into the eye, constriction of the vessels follows, but the permeability is not altered. The intraocular tension does not show any change and there is no evidence of any toxic action.

The curative effect of corvasympton cannot be attributed to its vasoconstrictory action. Burns treated with adrenaline in any concentration do not show any improvement. On the contrary, if adrenaline is instilled in a concentration higher than 1:1,000 the condition of the eye is made worse.

It is thought that the beneficial effect of corvasymton is due to the adrenalone which it contains. Adrenalone is dioxyphenyloxymethylaminoethanol



which is a keto form of adrenaline. It has been found (Loewi and Meyer, 1905; Dale, 1909) that adrenalone is much less toxic and has much less vasoconstrictory action than adrenaline. In solution of the latter the keto form of adrenalone is absent.

Besides the restoration of corneal transparency, the treatment of chemical burns of the eye has in view the prevention of adhesions between the conjunctiva and the ocular globe. As early as 1912 Denig removed the necrotic conjunctiva and replaced it by mucous membrane from the mouth. Thies (1928) again drew attention to the favourable effect of this treatment. However, in 1939, Passow noted that an oral mucosa graft was unnecessary, as the same results could be obtained by loosening up and undermining of the injured conjunctiva at the limbus corneae. In spite of its "necrotic" appearance, the conjunctiva is still capable of remarkable recovery.

In a chemical burn of the eye a deposit of the corroding agent is retained beneath the conjunctiva. Its gradual absorption, by impairing the nutrition of the sclera, cornea, and conjunctiva, gives rise to the well-known sequelae of chemical burns. By loosening up and undermining the conjunctiva at the limbus, the formation of a deposit is prevented and the subconjunctival tissue is laid open to the direct action of corvasymton.

I used to treat conjunctival and corneal chemical burns in the usual way—that is, by copious irrigation of saline solution or ammonium tartrate 10% solution; removal of all particles of the injurious material; frequent instillation of cod-liver oil, and insertion of a plastic contact glass to prevent formation of adhesions between raw surfaces. The most favourable cases took a long time to recover, and a completely clear cornea was an unusual result. In severe cases corneal opacities and wide adhesions were inevitable sequelae of the use of the contact glass.

I never had the opportunity to use tolazoline hydrochloride, which is a hyperaemia-inducing preparation recommended by Nagy (1951), nor transplantation of the oral mucosa (Denig–Thies operation).

The quick disappearance of the chemosis and the complete clarification of the corneal cloudiness and opacities which follow upon the frequent instillation of corvasymton, coupled with free loosening and undermining of the conjunctiva, are so impressive that this preparation may be regarded as a very important asset in the treatment of lime burns of the eye.

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POLIOMYELITIS IN CHILDREN UNDER 6 MONTHS IN ENGLAND AND WALES DURING 1950

BY

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Logan (1952) in his report on the distribution of poliomyelitis in England and Wales in 1950 stated that 82 cases of poliomyelitis were notified in children under the age of 6 months.

In correspondence with the medical officers of the districts in which these 82 cases occurred we found that in fact 5 were over 6 months old. Of these 2 were non-paralytic and 3 were paralytic. On the other hand, we were given information of 5 children who developed poliomyelitis during 1950 and were under the age of 6 months, but who were not included in Logan's figures. These 5 children had a paralytic attack. We have excluded the 5 children who were over 6 months of age and included the 5 referred to above. It is on this revised list of 82 cases that we are reporting the results of our investigation.

Logan's figures show that of the 82 cases that were notified in children under 6 months 72 were paralytic and 10 were non-paralytic. Our follow-up of the revised list of cases shows that 77 were paralytic (including the fatal cases) and 5 non-paralytic.

Our primary object was to consider: (1) the incidence of poliomyelitis in children under the age of 6 months; (2) its fatality, severity, and the extent of recovery; and (3) whether breast-feeding had any effect in preventing poliomyelitis.

Incidence

The incidence of poliomyelitis in children under 6 months of age was of particular interest to us in connexion with immunization against diphtheria, either alone or combined with a vaccine against whooping-cough; for Bousfield (1951) had suggested in 1951 that if children received their immunization earlier in infancy they would run less risk of contracting that type of paralytic poliomyelitis which is associated with immunization. It was assumed that this suggestion was based on the supposed infrequency of poliomyelitis in children under this age.

In children under 15 the total number of notifications of paralytic poliomyelitis in 1950 was 3,799. The number of children under 6 months per 1,000 children under 15 in 1950 was 35.8. The expected number of notifications in children under 6 months would therefore have been $\frac{35.8 \times 3,799}{1,000} = 136$. There were in fact 77 cases according to our investigations.

In the same age group there were notified 1,525 cases of non-paralytic poliomyelitis. On the same basis the expected number in children under 6 months would have been 54.5. There were in fact, according to our investigations, 5.

It would appear, therefore, that the incidence of paralytic poliomyelitis in infants under 6 months was approximately 56.6% of what it would have been had it been evenly distributed in six-monthly age groups in children under the age of 15, and for non-paralytic poliomyelitis 9%.

In our opinion: (1) These facts, together with the severity of the disease in this age group (see later) would not have warranted the continuation of immunization in 1950 in children under 6 months in a district where there was an outbreak of poliomyelitis, solely on the grounds that the children were under 6 months old. (2) Non-paralytic poliomyelitis is not frequently notified in children under 6 months. This may be due to (*a*) the difficulty of diagnosis of non-paralytic poliomyelitis in children under 6 months; and (*b*) the possibility that lowered resistance to the poliomyelitis virus in this age group results in almost all cases developing paralysis.

Mortality

Of the 82 patients we investigated 19 died, giving a mortality rate of 23%. We have compared this with the mortality rate of poliomyelitis in 1950 in persons over the age of 6 months. During that year there were 7,668 notifications in this age group, and of these patients 715 died, giving a death rate of 9.3%. It is therefore apparent that in 1950 the mortality rate of poliomyelitis in children under 6 months was more than double that of persons over this age.

Table I shows the mortality rate in three separate age groups for children under 6 months of age. It also indicates that for poliomyelitis in 1950 the younger the children the greater was the mortality rate. Table II gives the age of onset and death of the 19 fatal cases.

TABLE I.—*Fatality*

	M	F	Total	Died	Survived	Mortality
0–9 weeks ..	14	10	24	9 (F 4, M 5)	15	37·5%
10–18 „ ..	13	16	29	6 (F 3, M 3)	23	20·7%
19–26 „ ..	19	7	26	4 (F 0, M 4)	22	15·4%

We have had to exclude three children whose exact age we were unable to ascertain.

TABLE II

	Age at Onset of Poliomyelitis	Age at Death
J. F. T.	8 days	10 days
L. E. G. ..	13 „	20 „
S. H.	2 weeks	18 „
B. O.	4 „	46 „
A. R.	5 „	6 weeks
P. H.	6 „	6½ „
M. J. G.	7 „	9 „
C. G. B. ..	7 „	20 „
E. R.	8 „	8 „
U. J.	12 „	13 „
A. A.	12 „	12 „
J. S.	16 „	16 „
D. R.	16 „	16 „
J. P.	17 „	17 „
K. B.	18 „	18½ „
T. G.	19 „	19 „
R. D. A. ..	22 „	22½ „
K. G. C. ..	23 „	23½ „
S. S.	23 „	23 „

These figures are an additional indication of the severity of paralytic poliomyelitis in the early weeks of life. It will be seen that in most cases death ensued within a question of days from the onset of the disease.

The mortality of poliomyelitis in young babies has been reported upon by Smallpeice and Ounsted (1952). They describe an outbreak of poliomyelitis in a nursing-home. The patients were infants aged 7, 3, and 2 weeks respectively. Two died and one is an epileptic idiot with palsies and athetosis. It is interesting to note that these authors state that all forms of poliomyelitis are uncommon in early infancy, quoting Mouton, Smillie, and Bower (1950). This statement was not borne out in the 1950 epidemic in England. We have also information of an outbreak in a maternity home in 1952. Three newborn babies contracted poliomyelitis and two died.

We would refer to the report of an outbreak of poliomyelitis in Israel in 1951 (Health Services of Israel, 1952). Of 1,602 cases notified 30% were in children under 1 year of age. We have not yet received information concerning the actual ages of the children, nor the death rate in monthly or quarterly age groups.

Severity and Recovery

For the purposes of this review we have classified our cases as fatal, paralytic, and non-paralytic. Of the 82 cases, 19 were fatal, 58 paralytic, and 5 non-paralytic. We have classified the extent of paralysis in the paralytic cases as follows: A, three or more limbs or two limbs and one other part of the body affected. B, two limbs or one limb and one other part of the body affected. C, one limb affected. R, complete recovery.

Table III sets out the extent of paralysis in 55 of the 58 paralytic cases. In three cases we did not succeed in obtaining information about the initial extent of paralysis and the condition three years later.

TABLE III

Initial Paralysis		Condition 3 Years Later			
		A	B	C	R
A	18	8	6	3	1
B	12	—	4	7	1
C	25			16	9
Not known ..	3	—	—	—	—
Total	58	8	10	26	11

We have not been able to make a scientific comparison between the severity of the disease in children under 6 months and the severity at all ages in 1950, for we have no comparable figures. We can only draw attention to the fact that 19 children died and that 18 were very severely paralysed. On the other hand, dealing with the question of recovery, we would confirm our opinion, previously expressed, that in poliomyelitis recovery is to some extent proportionate to the initial severity of the paralysis of the affected limbs (Geffen, Paterson, and Tracy, 1953).

Breast-feeding

Dr. S. K. Sanders, in a personal communication, gave us some information concerning mouse encephalomyelitis virus, which behaves in some ways in the same manner as the poliomyelitis virus. Female mice which have a high degree of circulating antibody as a result of active immunization transfer this immunity to their offspring via the colostrum and milk. Suckling mice of such mothers are correspondingly more resistant to peripheral challenge with active virus than the offspring of mothers who have not been so immunized. This is also true of the Coxsackie virus.

It was with this in mind that we determined to inquire into (1) the history of the mothers of the 82 children, with a view to ascertaining if they had had any recent attack of poliomyelitis; and (2) the extent to which the 82 children were breast-fed.

(1) In 76 of the 82 cases we could obtain no history that the mother had at any time suffered a diagnosed attack of poliomyelitis. In the remaining six cases the mother and the child both developed poliomyelitis either simultaneously or within a few days of each other. Further details of these six cases are given below.

(2) Of the 19 children who died, 4 were being entirely breast-fed at the time of death; 8 had been breast-fed for varying periods; 4 had never been breast-fed; and in the

remaining 3 cases we could obtain no information. Of the children who survived, 15 were entirely breast-fed; 32 had been breast-fed for varying periods; 10 had never been breast-fed; of 6 we could get no history.

Thirteen children developed poliomyelitis under the age of 6 weeks—6 died and 7 survived. Of the 7 survivors, 5 were entirely breast-fed, and, of these, 3 had a mild attack (category C).

In the absence of a history of poliomyelitis in the mother, or knowledge of whether she had had an undiagnosed attack, we are unable to make any deductions of value from these figures.

The following are the details of the six cases in which the mother also had poliomyelitis.

Case 1. J. F. T.—The mother died of poliomyelitis six days after the baby was born. This baby died of poliomyelitis at the age of 10 days.

Case 2. R. H. H.—The mother died of poliomyelitis on the fifth day of the puerperium. The child developed poliomyelitis at the age of 10 days and had a very severe attack (category A).

Case 21. A. D. T.—The mother contracted an abortive attack of poliomyelitis at the same time as the child. The child—aged 9 weeks—contracted a serious attack of poliomyelitis (category A).

Case 33. O. H. G.—The mother contracted an abortive attack of poliomyelitis at the same time as the child. The child contracted poliomyelitis at the age of 13 weeks and had a serious attack.

Case 39. S. F.—The mother had a severe attack of poliomyelitis seven days before the child. The child contracted poliomyelitis at the age of 15 weeks and had a mild attack.

Case 51. A. B.—The mother had poliomyelitis two days before the baby. The child developed poliomyelitis at the age of 17 weeks and had a mild attack (category C).

History of Immunization or any Operative Procedure

We inquired in every case whether the child had been immunized or subjected to any operation. In view of the fact that all the children were under 6 months it is not surprising to find that only one of them had been immunized, and this was against whooping-cough. The injection was in the right arm, and took place six to eight weeks before admission to hospital. Paralysis was limited to the left leg.

Only one child had been vaccinated against smallpox. Vaccination took place at the age of 4 weeks, and the child contracted poliomyelitis at the age of 22 weeks. This case (R. D. A.) was fatal.

One child (B. O.) had an operation for pyloric stenosis on August 4. On August 14 the mother noticed that the child had difficulty in breathing. He was readmitted to hospital on the 17th and died on the 18th.

Pre-paralytic Symptoms

In view of the difficulty of diagnosis of poliomyelitis in infants, we have attempted to assess the importance of the pre-paralytic symptoms which have been recorded. Table IV sets out the position.

TABLE IV.—*Pre-Paralytic Symptoms*

Nil	11
Not known	9
Drowsiness alone or associated with other symptoms	15
Pyrexia, either alone or associated with other symptoms	21
Irritability	4
Abdominal symptoms such as loss of appetite, pain, diarrhoea, and vomiting	8
Other symptoms	11

We are of the opinion, judging from the above Table and from the reading of individual case sheets, that in this series there were no definite pre-paralytic symptoms diagnostic of poliomyelitis; they were rather symptoms of any acute infection in the first six months of life.

Summary

A report is presented of 82 cases of poliomyelitis in children under 6 months which occurred in England and Wales during 1950. Of the 82 cases, 77 were paralytic and 5 non-paralytic.

The incidence of paralytic poliomyelitis in infants under 6 months was 56.6% of what it would have been if such incidence had been equally distributed in six-months age groups in children under 15 years.

Non-paralytic poliomyelitis is infrequently diagnosed in children under 6 months.

The overall mortality rate was 23%, and this mortality increased as age diminished. In children under 9 weeks the mortality rate was 37.5%.

Of the 58 paralytic cases who survived, 30 were either very severely or severely paralysed, and of these only 2 made a complete recovery.

We have discussed the influence of breast feeding on the incidence and course of the disease.

The pre-paralytic symptoms were not diagnostic except of an acute infection in a child under 6 months.

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Medical Memoranda

Acute Strychnine Poisoning after a Massive Dose

Deaths from strychnine poisoning are not uncommon and have been exhaustively dealt with in the literature. The interest of the present case lies in (*a*) the enormous dose which must have been taken and the rapidity with which death occurred; (*b*) the little evidence of any of the classical symptoms of strychnine poisoning; and (*c*) the further evidence of the extreme rapidity of absorption of the drug from the alimentary canal.

CASE REPORT

The deceased was a pharmacist aged 56. At 10 o'clock one morning, having dispatched all but one of his assistants on various errands, he retired to a room over the shop. Eighteen minutes later he was found in this room by an assistant, lying on a couch with his head on the seat and his legs dangling over the raised end. Examination by a doctor five minutes later proved life to be extinct, and it seems probable that he was already dead at 10.18, when found by the assistant. There is good evidence, therefore, that death ensued at the most 15 minutes after swallowing the poison, and probably rather less. When the body was examined by the doctor there was no trace of any muscular rigidity. It is probable that if there had been any violent convulsions before death the man would not have remained on the couch but would have rolled off on the floor. Beside the body was found a partly filled bottle of solution of strychnine hydrochloride, and crystals of what later proved to be strychnine hydrochloride were found in the deceased's mouth, down the front of his pullover, and on the floor surrounding the body.

The necropsy findings were largely negative apart from rather meagre evidence of asphyxia.

The viscera were subjected to the classical Stas-Otto extraction. The residues from the chloroform–caustic-soda extraction were heated on a water bath for 30 minutes with concentrated sulphuric acid, diluted with water, filtered, made alkaline, and re-extracted with chloroform. Removal of the chloroform yielded a white, crystalline, weighable residue which was proved to be practically pure strychnine by melting-point determination and titration. This last was effected by dissolving the residue in 0.01N sulphuric acid and back-titrating with 0.01N caustic soda, using methyl orange as an indicator. From the titration figures the fol-

lowing amounts of strychnine hydrochloride were calculated to be in each organ : liver, 125 mg. ; kidneys, 30 mg ; bowel, 4,608 mg. ; stomach and contents, 653 mg. ; blood, 4 mg. per 100 ml. ; urine, trace.

If we assume a circulation volume of 5 litres the total amount of strychnine in this would be 200 mg. There is, therefore, a total recovery of about 5.6 g. (84 gr.) of strychnine from the main viscera. It was estimated that the deceased had consumed 12 fl. oz. (340 ml.) of solution of strychnine hydrochloride (containing about 53 gr. (3.4 g.) of strychnine hydrochloride), but the amount of crystalline strychnine hydrochloride taken was not known.

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Primary Carcinoma Simulating Empyema of the Gall-bladder

Primary carcinoma of the gall-bladder is the fifth or sixth in order of frequency of cancers of the alimentary system. It is found in from 1 to 2.6% of all gall-bladder operations, in 0.42% of all necropsies, and in 2.8% of all cases of malignant disease. These figures are given by Illingworth (1935), who studied 50 cases. Judd and Gray (1932), Lichtenstein and Tannenbaum (1940), Kirshbaum and Kozoll (1941), Vadheim, Gray, and Dockerty (1944), Benjamin (1948), and Sainburg and Garlock (1948), and other American surgeons have all reported numerous examples. The following two cases, however, seem remarkable enough to warrant publication.

CASE 1

A compositor aged 78 was admitted on July 5, 1949. He had been well until a fortnight before, when he noticed a dull aching pain between the shoulder-blades. This persisted for a week, when he visited his doctor, who found he was jaundiced. He then admitted that his urine had been dark in colour for about 10 days. On examination the liver was palpable two fingerbreadths below the costal margin and the gall-bladder was felt below it.

On July 14 the serum bilirubin was 22.4 mg. per 100 ml. ; blood cholesterol, 380 mg. per 100 ml. ; blood urea, 25 mg. per 100 ml. ; thymol turbidity, 1 unit ; colloidal gold, 0 ; alkaline phosphatase, 64 units ; serum protein, 6.4% (albumin 2.9%, globulin 3.5%). On July 29 the abdomen was opened through a right paramedian incision. Several pints of ascitic fluid escaped. The liver was cirrhotic and the gall-bladder large and tense with a sugar-icing surface. The gall-bladder was opened and cheese-like material removed with a spoon. It was excised with difficulty and a T-tube was placed in the common bile-duct. The patient became drowsy after the operation, gradually weakened, and died on July 31, 26 days after admission. Biliary cirrhosis, thrombosis of the hepatic vessels with patchy necrosis, and some metastases in the liver were found at necropsy.

Pathology.—The gall-bladder was 9 cm. long and 5.5 cm. in diameter. It was completely filled with yellow cheese-like material. Microscopically, no normal mucosa was seen. The wall was infiltrated by an ill-differentiated adenocarcinoma, which was forming acini in some places and not in others. The nuclei were large and vesicular with prominent nucleoli. There was very little mucin production. The material in the lumen had the structure of necrotic tumour and contained some pyknotic nuclei.

CASE 2

A secretary aged 52 first attended as an out-patient on December 11, 1950, complaining of bouts of pain between the shoulder-blades and on the right side of the abdomen, with occasional pain on the left side. She had always had to be careful what food she ate, but had never been jaundiced. On examination she was seen to be of sallow complexion. A swelling was felt below the ribs on the right side, and on January 3, 1951, a cholecystogram showed no filling of the gall-bladder. On February 5 the abdomen was opened by a right paramedian incision and a greatly enlarged gall-bladder presented. It was slightly inflamed, and the many adhesions were divided. Because of the size of the gall-bladder, a retrograde cholecystectomy was performed and the abdomen was closed with a drain. On February 20 the patient was discharged from hospital, having made an uneventful recovery. She was seen last on September 5 of that year, when she complained of occasional attacks of pain, but on examination nothing abnormal was found.

Pathology.—The gall-bladder weighed 460 g. and was 17.5 cm. long and 7 cm. in diameter. The surface in contact with the liver was 8.5 by 6 cm. Large veins coursed over its surface. It was filled with grey cheese-like material, which when washed away from the wall left a shaggy lining. There were 20 mixed faceted calculi ; the largest, 1.5 cm. in diameter, was impacted in Hartmann's pouch. There was a thickening up to 0.5 cm. of the wall of the organ on the ventral surface 5 cm. from the fundus. Microscopically, the contents of the gall-bladder could be demonstrated as masses of necrotic cancer. A section of the thickened wall showed a columnar-cell papillary adenocarcinoma growing in long trabeculae in a fine stroma. The cells were producing a little mucus and had large dark-staining nuclei with frequent mitoses. The wall of the gall-bladder did not appear to be completely penetrated by tumour at any point, and a section of the cystic duct showed no neoplastic tissue.

DISCUSSION

In both these cases, following a short history of symptoms referable to the biliary tract, a laparotomy was performed, and a grossly enlarged gall-bladder filled with cheese-like material was removed. In neither case was a diagnosis made until microscopical examination revealed an adenocarcinoma growing into the lumen of the organ. The cheese-like material was necrotic cancer, and there was no evidence of infection. Illingworth (1935) observed that the papillary type of carcinoma might reach a considerable size, partly filling the gall-bladder. It was prone to haemorrhage and necrosis, and might be so soft as to be mistaken for inspissated pus. In the series of 48 cases examined by Cooper (1937) 12% had papillary tumours, and some of these distended the gall-bladder. Rhodes and Greenblatt (1937) describe obstruction of the cystic duct by tumour as a cause of distension of the gall-bladder, which may simulate an empyema, but they make no mention of the organ being filled with necrotic tumour. Vadheim, Gray, and Dockerty (1944) found that 26 of their 77 cases had gall-bladders distended to four times the normal size, but the largest carcinoma they encountered measured only 7 by 6 by 5 cm. It is interesting to note that in 17 of their cases the carcinoma was limited to the mucosa and submucosa without penetration of the muscularis.

It therefore appears that the two tumours described are very large examples of a type recorded by some authors, but by no means universally recognized. A grave error would be made if cholecystostomy were performed in such a case.

My thanks are due to Mr. Ralph Shackman and Mr. Rodney Smith for permission to publish the cases and to Professor T. Crawford for his assistance in preparing the paper.

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Reviews

A PHILOSOPHY OF LIFE

The Natural History of Infectious Disease. By Sir Macfarlane Burnet, M.D., F.R.S. Second edition. (Pp. 356. 22s. 6d.) Cambridge: The University Press. 1953.

In 1940 Sir Macfarlane Burnet gave us a work entitled *Biological Aspects of Infectious Diseases.* This volume is described as its second edition, yet since the original work was written so many advances have been made in attacking the problems of infectious disease that the book has not only been given a new title but has been practically rewritten. It is not too high praise to term Sir Macfarlane's excellent book a philosophy of life, for it is written as Aristotle himself might have described the discoveries of modern science, and it is impossible to improve upon the Greek approach to the study of natural phenomena.

Under biological considerations the ecological aspect of infectious diseases, so important in epidemiology, and the evolution of infection and disease are examined. The aggressors—bacteria, protozoa, and viruses—are described. The chapter on viruses crystallizes modern research on the subject. How real these formerly hypothetical organisms have become is demonstrated by the frontispiece to the book, which shows the brick-shaped granular forms of the vaccinia virus as revealed by the electron microscope. Discussing the origin of these foes of men, animals, and plants, the author says that most research workers prefer the theory that animal viruses are the diminished descendants of pathogenic bacteria or protozoa.

Next come the processes of defence. After recounting the normal defences against bacterial infections and the development of immunity after disease, its chemical basis, antibodies, and its wider significance, the author examines "what makes bacteria dangerous," and reminds us that, even to-day, probably more than half of all human deaths are due essentially to micro-organismal invasion. Except for certain abnormally fatal epidemics, the state of the host is more important in determining the outcome than is the virulence of the micro-organism. Hence the importance of healthy living and adequate nutrition. He then describes the natural history of infectious disease—how infections spread, the transfer of infection from one species to another—animal reservoirs, the general character of epidemics, the prevalence of infectious disease, endemic epidemics, age-incidence of infectious disease, immunity as an epidemiological factor, the general principles of controlling infectious disease, together with an account of the antibacterial drugs, which within the short space of a decade have shorn many deadly diseases of their terrors and paved the way for the eradication of others.

A section of the book is devoted to the study of certain important diseases—diphtheria, influenza, plague, cholera, malaria, and yellow fever. Finally, the grave problem of atomic warfare and the use of micro-biological weapons are discussed. The outlook is indeed gloomy if mankind is destined to destroy civilization through its scientific discoveries.

This is a book which should be read by doctors, men of science, health administrators, and politicians. It emphasizes the recent warning of Professor A. V. Hill that every scientific and medical discovery brings with it human problems to solve—moral, social, political, or aesthetic. Scientific and technical progress cannot alone solve the problems of humanity. "That belief is magic and magic of the unattractive sort that denies a place to the human spirit."*

ARTHUR S. MACNALTY.

*Address delivered at the annual assembly of faculties of University College, London, on July 2, 1953.

FOUNDER OF THE RED CROSS

Man Born to Live: Life and Work of Henry Dunant, Founder of the Red Cross. By Ellen Hart. With preface by H.R.H. the Princess Royal, and an introduction by Paul Ruegger, President of the International Committee of the Red Cross. (Pp. 371. £1 2s. 6d.) London: Victor Gollancz. 1953.

Many, perhaps most, people do not know that Henry Dunant was the man chiefly responsible for the Red Cross movement and the Geneva Convention. The reason for this is that he was really not a strong or very admirable character. The story of his life is well and faithfully told in this book, which will attract many readers.

Henry Dunant was born in 1828 in Geneva and was a "mother's boy" to such an extent that the maternal influence "set him back and for the rest of his life he was lacking maturity in some of its aspects." In his youth he was an earnest evangelical Christian. He entered the service of a bank and willingly went to Algeria, where he thought he might combine business with evangelism. There he started a private business venture, left the bank, and tried to obtain influential support for his enterprise. He was a good talker and had a most persuasive manner. In attempting to obtain support from the Emperor Napoleon III he followed the latter to the battlefield of Solferino, where he was so moved by the horrible sights he saw that for a time he did good work in succouring the wounded. In 1862, under the influence of strong emotion, he wrote *Un Souvenir de Solferino,* in which he included views which were to lead to the formation of the Red Cross organization. He sent copies of this work to many influential people, including the crowned heads of Europe. The ideals set forth therein were supported by a committee formed in Geneva, and Dunant's personal and sometimes irresponsible efforts spread its influence, but his financial ruin, which involved many of his relatives and friends, compelled him to leave his native city. For many years he lived in comparative obscurity, but in later life his pioneer work was recognized and he obtained a Nobel award. He died at the age of 82.

There is no doubt that Dunant was a man inspired by high ideals and able to move others along humanitarian lines, but he worked "by instinct and emotion," and some of his projects were unpractical if not hare-brained. He was an individualist who described himself as "the dupe of a burning imagination, of an over-impressionable temperament," and he seems to have been a poor man of business. Nevertheless he impressed a great humanitarian idea on those who held the reins of authority in Europe, and for this we must hold him in honour.

ZACHARY COPE.

DIABETES

Die Zuckerkrankheit: Diagnose, Klinik, Pathologie, und Therapie. By Professor Ernst Wiechmann. (Pp. 318. M. 28.50.) Munich: J. F. Lehmanns Verlag. 1953.

After a silence of many years three large books on diabetes have appeared in the German language in the last three years. This one by Professor Wiechmann is voluminous and comprehensive. His foreword states that he started to write it in 1929 and has been absorbed in the subject ever since. The effect of this is obvious, and he has not criticized and excluded sufficiently the older references he gives. He lists some 2,000 references, arranges them well in an addendum, but gives the reader no critical evaluation of their contents. Much of the later work he quotes disproves the validity of the earlier. Great historical thoroughness, but too much of it is out-dated and useless. And, as an author quoted, I am a little sad to find that the last edition of my book was produced in 1927 and not, as in fact, in 1951.

The author addresses his book to *all* students and doctors, and makes a true point in his preface. He points out that diabetes affects all branches of medicine and surgery in a

special way of its own—from eyes, liver, nervous system, to feet—and so it behoves all general doctors and specialists to know its widespread effects. This is so true that all should ponder it.

The book covers all these aspects very well. But it gives insufficient help in practice to any doctor who wants to know how to use insulin and its different types or how to treat diabetic coma. The recommendation to give glucose, fructose, and saline by rectum requires changing.

R. D. LAWRENCE.

NERVE-ROOT CYSTS

Sacral Nerve-Root Cysts: Another Cause of the Sciatic or Cauda Equina Syndrome. By Professor I. M. Tarlov, M.D. (Pp. 134; 65 figures. £2 7s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

This short monograph by the professor of neurology and neurosurgery at the New York Medical College is of considerable interest. Some years ago he made a study of the histology of the filum terminale, and in the course of dissecting 30 cases he found perineural cysts of the posterior-sacral nerve roots and ganglia in five. These cysts, which arise at the junction of the dorsal root and ganglion, vary in size up to 3 cm. in diameter and may be multiple. They do not communicate with the subarachnoid space, and are disclosed only when the posterior sacral arch is removed. At first the author regarded these cysts as pathological curiosities without clinical importance, but in 1947, when operating on a patient with sciatica, the suspected protrusion of an intervertebral disk was not found. On removing part of the posterior arch of the sacrum a cyst was seen on the second sacral root, and after the cyst had been removed the patient was relieved of sciatic pain. Professor Tarlov has subsequently operated on three further patients in whom similar cysts were causing symptoms either of sciatic pain or of disturbance of function of the lower sacral roots, and he mentions in detail three patients treated by other surgeons.

The author gives an excellent illustrated account of the naked-eye and histological appearances of these perineural cysts and discusses their possible aetiology. As a clinical account and a guide to the best method of treatment, it must be regarded as a preliminary report owing to the small number of cases so far recognized. But the author has probably drawn attention to a condition of clinical importance, and the monograph is well worth the attention of anyone interested in sciatica and in disturbances of the cauda equina.

J. W. ALDREN TURNER.

THE MIND MADE EASY

Psychology Without Tears. By William O'Connor, L.M.S.S.A.(Lond.), D.P.M.(Lond.). (Pp. 220. 12s. 6d.) London: Rider and Co. 1953.

The lay public has in these days a great appetite for popular psychology in plays, lectures, and books. It delights in being made aware of how people think and how reassuringly commonplace are its own secret thoughts. Interest in the subject is no longer confined to the lunatic fringe of society and to those with pretentions to intellectualism. The conscious application of psychological knowledge and theory is considered a legitimate part of the conduct of life by the diplomat, the salesman, the seducer, or the schoolboy who wishes to extract a tip from a rich uncle. A good deal of sharp practice can, in fact, be rationalized in the name of psychology. One of its most important applications, on the other hand, is that a knowledge of mind can turn mere good will into informed kindliness, and nowhere is this more important than at the bedside.

If psychology is to be learned without tears—and tears are here a symbol for the painful effort of concentrated thought—there can be no atmosphere more congenial than that of the dinner-table, and Dr. Connor's style has the easy flow of the man who has, by general consent, monopolized the conversation. A sententious opening and evidence here and there of a moralizing tendency detract very little from a survey of those parts of the subject which are likely to be of interest to the mentally healthy and inquiring layman.

The approach is singularly free from the bias of any particular school of thought, and gives little encouragement to morbid introspection, and the patient who asks for a "book on psychology" will come to no harm if he reads this one. Other popular writers in this field might have chosen different aspects of the subject, might have been more profound, but would probably have been far less readable.

ALEXANDER KENNEDY.

THE OESOPHAGUS

The Esophagus and its Diseases. By Eddy D. Palmer. (Pp. 553; illustrations by Phyllis Anderson. £4 13s.) London: Cassell and Co. 1953.

This book of 553 pages describes first the anatomy and clinical physiology of the oesophagus, and then in the twenty-five following chapters covers all the common and uncommon groups of disorders or diseases of the oesophagus. Each chapter is followed by a lavish bibliography.

The book has a useful collection of references, but even so it is curiously incomplete. No one in Britain writing about hiatus hernia would omit Harrington's contributions from the U.S.A., and yet Allison's work, of similar scale and importance in this country, is not mentioned in the book. Similarly, in writing about atresia of the oesophagus, British writers would properly refer to Sweet and Swenson, yet corresponding work by Franklin in Britain has been overlooked.

It is difficult to believe that this book is representative of American views. Operations for anastomosing the stomach and oesophagus for achalasia have ceased to be done in Britain but are advocated in this book. Heller's operation is scarcely mentioned. Many patients with hiatus hernia derive much relief from raising their shoulders on pillows at night or by raising the head of the bed on blocks, but in this book we are merely told that "certain simple postural measures would be helpful if they did not interfere to an excessive extent with normal living." Throughout the book the reader is lost in a forest of references and his therapeutic route is dimly marked. It is curious that there should be no section on the investigation of oesophageal diseases by oesophagoscopy or radiology. The book will be of interest to those whose work brings them particularly into contact with this branch of medicine or surgery, but for the general physician or surgeon it is dangerously misleading and is not recommended.

F. AVERY JONES.

CONTACT LENSES

Contact Lens Routine Practice. By Norman Bier, F.B.O.A. (Hons.), F.A.A.O., D.Orth. Foreword by F. A. Williamson-Noble, F.R.C.S. (Pp. 188; 105 figures. £2 2s.) London: Butterworth Scientific Publications. 1953.

This is a short practical book on the theory and practice of contact lenses. This comparatively new form of optical correction is rapidly becoming popular, and, although it is probably true that the day of basic discoveries has now ended, new improvements in technique are constantly being suggested. Among these full-clearance perforated (or ventilated) lenses, sealed minimum-clearance lenses, and corneal lenses without the usual supporting rim resting on the sclera are fully discussed, and their advantages and disadvantages assessed in the light of the author's considerable experience. He unhesitatingly prefers perforated contact lenses in preference to the sealed types in all but exceptional cases, as, for example, marked conical cornea. He presents clearly the technicalities of the subject and gives much detailed and sound practical advice on fitting the lenses and on their wear and aftercare by patients. The illustrations are unusually clear and informative.

STEWART DUKE-ELDER.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY AUGUST 22 1953

BACKWARD READERS

Illiteracy is a much more complicated subject than might be thought from the many confident statements made about it nowadays. Some figures particularly liable to misinterpretation have recently been issued by the Director of Army Education. They were in a survey of the numbers of "illiterate" and "sub-illiterate or backward" recruits among some 45,000 National Servicemen. The percentage of backward recruits is given as 23, though it ranges from 6% to 45% in different counties.

In the interpretation of such figures much depends on the criterion or test used to measure reading ability. Here the tests were arithmetical and verbal. The illiterates, who totalled 1.2%, were those who could not fill in the answers to a set of simple questions about personal particulars. If we defined illiteracy as inability to read aloud or as a person's inability to understand what he is reading, the results might differ. Again, people do not fall into distinct classes; rather there is a continuous gradation from superior to minimal educational attainment. Hence the proportions of backward or illiterate persons will depend on where an arbitrary line is drawn, and the Army's figure of 23% is meaningless without precise definition of the degree of backwardness to which it refers. The corresponding number below this borderline early in the war was about 15%, and it must be admitted that there has been a decline in educational standards over the war years which has not yet been made up. The figure of 1.2% illiterate also needs interpretation, though for a different reason. In general, Army recruits constitute a fairly representative sample of the young adult male population, but at the bottom an unspecified number are rejected at recruiting centres on medical or psychological grounds, and if these were included the proportion of illiterates would certainly be higher. Even so the results tend to confirm the careful survey published in 1950 by the Ministry of Education,[1] where it was shown that illiterate school-leavers and young adults amounted to about 1% of their group. Illiteracy was there defined as reading comprehension poorer than that of average 7-year-old children in 1938. The survey also showed that the proportions of backward readers (with a "reading age" less than 12 years by 1938 standards) were 30% among 15-year-olds and 17% among adults.

Many of the figures that the Army gave for different counties must be treated with great caution because the numbers are small, but at least some of the differences between larger groupings are significant. Thus Welsh counties show 32½% of "backwardness," Scottish ones only 19½%. The latter figure probably reflects the greater emphasis on mechanical drill in arithmetic at Scottish schools, while the former is obviously affected by the difficulties of Welsh-speaking recruits with an English-language test. There is apparently more backwardness in rural than in urban areas, for the most populous counties usually, though not always, get the best percentages. There are other difficulties, seldom recognized, in the interpretation of the figures which many education authorities are collecting in response to the present public outcry about illiteracy among school-leavers. Some, for example, usé tests which are based either on 1918 or on 1948 standards, and these naturally give a more gratifying picture than tests based on 1938 standards. Again, the business man who complains of the illiteracy of his office-boys and typists has overlooked the change in occupational distributions during the past 30 to 40 years. Far more of the brightest and best-educated adolescents nowadays enter skilled engineering or administrative and professional services, and employers often have to go much further down the scale of intelligence than they used to do.

Though the question how much illiteracy there is in the population is impossible to answer, the serious fact is that the proportion of backward individuals in Britain (on any criterion) is greater than before the war. In other words, average educational standards have fallen. Explanations of this are highly controversial and difficult to prove or disprove. That there has been a general decline in national intelligence, as forecast by eugenist writers, is not borne out by the Scottish Council for Research in Education's investigations. Often the blame is cast on modern educational methods. Here, too, the only available scientific evidence is negative; children educated in good "progressive" schools reach as high attainments as those taught in more "orthodox" schools. But it may still be true that some so-called progressive methods are slipshod and ineffective. Even so,

[1] *Reading Ability*, Pamphlet No. 18.

Sir Cyril Burt has found that much the most frequent causes of educational backwardness are, first, lack of intelligence, secondly, unfavourable home circumstances, and, thirdly, emotional maladjustment, anxiety, and lack of confidence. Poor teaching methods or school organization are only occasionally prominent. It would seem that the main reasons for the decline were wartime upsets such as bombing and evacuation, large classes, frequent changes of staff, and unsettled home conditions. Several of these still exist. For example, because of the high birth rate just after the war, the schools must for another ten years take more pupils than they are fitted for. No one knows whether certain home factors may not be more important—for instance, a decline in parental responsibility or increases in cinema-going and radio-listening or viewing. There is still much ground to be regained before achieving even pre-war standards.

TRAUMATIC EPILEPSY

When the Military Hospital for Head Injuries at Oxford was started in the early part of the war one of its purposes was the collection of well-documented case histories for research purposes, and since the end of the war a Head Injury Advice Bureau has kept in touch with many of the patients. Ritchie Russell and Whitty have made use of this material in a study of traumatic epilepsy, of which the first two papers have been published.[1,2]

Here they have considered only penetrating wounds of the brain. The occurrence of a single epileptic fit or focal attack put the case into the category of traumatic epilepsy, though some patients who had attacks about which too little was known were not classified as epileptic. Of 820 survivors of penetrating brain wounds, 43% have developed epilepsy within five years of the wound. Among the 464 patients who have not developed epilepsy, 61 have been followed up for less than five years, and the probability is that some of these men may also become epileptic in the future. It is well recognized that epilepsy may start later than five years after an injury. In Ashcroft's[3] first war series fits started at a later date in 10% of the cases, and therefore the eventual incidence of post-traumatic epilepsy in the series is likely to be higher than 43%. However, in over half the cases fits are infrequent and are not in themselves causing serious disability. Figures from the first war are similar. Ashcroft, using Ministry of Pensions records, found a 45% incidence in 129 cases, and in other series the figures have been 44% of 562 cases[4] and 49.5% of 1,234 cases.[5] It is disappointing to find much the same incidence in the two wars, for it was hoped that the earlier surgery practised in the last war, the better wound debridement, and the reduction of infection with less scarring as a consequence would diminish the incidence of this complication. But some severely wounded patients may have survived who might have died of their wounds in the first war. This comparable incidence of traumatic epilepsy is some evidence against the idea that an important cause of the epilepsy is progressive scarring in the brain. As the authors point out, the incidence is very similar to that of epilepsy occurring after a brain abscess (50%).[6] Referring to what they call this one-to-one ratio between patients who do and do not develop epilepsy, they consider that it points to "a balance of two equally important factors which may swing towards or against epilepsy developing, according to which of the two factors is most damaged."

As in previous reports[3,7] there is a higher incidence of epilepsy with wounds in the central part of the brain than with wounds towards the poles, but the authors have made the new observation that wounds within 5 cm. of the sagittal line have a statistically much lower incidence of traumatic epilepsy than wounds elsewhere in the brain.

The second paper is devoted to a study of focal motor and somatic sensory fits, including fits which start focally and become generalized later. These form by far the largest group of focal epilepsies in the series, and the observations are based on 85 cases. A number of interesting points have been brought out here. A fit starting with a sensory aura and then showing clonic movements is common, but it is very rare for the reverse spread from motor to sensory phenomena to occur. In only one patient were focal clonic movements followed by numbness, and in a few others by the uncommon epileptic phenomena of sensations of heat or of pain. It is also rare for one type of sensory aura to change to a different sensory aura.

From these two observations the authors suggest that the cortical cells concerned with sensation have easier anatomical access to the motor cortex than to post-central cells concerned with other types of sensation. Inhibitory epileptic attacks—and the authors suggest that numbness is the sensory counterpart of an inhibitory motor fit—tend to affect larger

1 *J. Neurol. Neurosurg. Psychiat.*, 1952, **15**, 93.
2 Ibid., 1953, **16**, 73
3 *British Medical Journal*, 1941, **1**, 739.
4 Baumm, H., *Z. ges. Neurol Psychiat.*, 1930, **127**, 279.
5 Credner, L., ibid., 1930, **128**, 721.
6 Jooma, O. V., *et al.*, *J Neurol. Neurosurg. Psychiat.*, 1951, **14**, 308.
7 Turner, W. A., *J Neurol Psychopath.*, 1923, **3**, 309.
8 Penfield, W. G., and Krestiansen, K., *Epileptic Seizure Patterns*. Springfield, Illinois: Charles C. Thomas. 1951.

areas of the body than clonic motor or positive sensory attacks. This agrees with the experimental findings in monkeys that stimulation of suppressor areas tends to cause widespread rather than local motor inhibition. But there seems to be little evidence for the authors' suggestion that post-epileptic paralysis is due to involvement or release of some inhibitory mechanism rather than the more usually accepted view that it is an exhaustion phenomenon. One other observation is of importance. It is that clonic focal attacks are more frequent with small Rolandic wounds with a slight permanent sensory-motor deficit than with extensive wounds causing a severe hemiplegia. This undoubtedly supports the view that the cortex is specifically concerned with clonic movements.

These detailed clinical studies of the course of the epileptic fit in a series of cases where the extent of brain damage is fairly accurately known are of great value, especially when considered in relation to the results of electrical stimulation of the exposed human brain.[8] Further reports on the more complicated fits with auras relating to the special senses, to speech, and to the body image will be awaited with interest, and of special importance will be the authors' final conclusions on the cause of traumatic epilepsy.

WORLD CONFERENCE ON EDUCATION

The First World Conference on Medical Education takes place in London next week. The British Medical Association is acting as host organization and will welcome to its Headquarters the many hundreds of visitors, from overseas as well as from Great Britain, who are meeting to exchange their diverse ideas and experience on undergraduate medical education—the main theme of the Conference. It is being held under the auspices of the World Medical Association, and the World Health Organization has lent a helping hand from an early stage; much support has also been received from the Council for International Organizations of the Medical Sciences and the International Association of Universities. Sir Lionel Whitby, the President, will be supported by Professor W. Melville Arnott as Deputy President, and, as Vice-Presidents, Professor A. Hurtado (Peru), Dr. Victor Johnson (U.S.A.), Sir Arcot L. Mudaliar (India), and Dr. A. Stampar (Yugoslavia), the last-named having taken the place of Professor René Sand, whose enforced absence through illness is much regretted.

The great variety of topics to be discussed at the Conference will make it of wide appeal to doctors, and it is hoped that as many as possible in this country will be able to take some time off, even if only a day or so, to make their contribution to discussing what Sir Lionel Whitby describes as "the dominant problem facing the medical profession in the second half of the twentieth century"—the problem of medical education. He asks how, in an age of ever-increasing scientific advance and ever-increasing specialization of knowledge, we can best teach the young men and women who will be the doctors of the future. This is the challenge before the Conference. While no final answer can be expected, the great range of subjects to be debated and the participation of distinguished men from all over the world give promise that the first large-scale attack on the problem will carry far.

Registration takes place in the Registration Bureau of the Conference, Great Hall, B.M.A. House. The Bureau will be open between the following hours: Saturday, August 22, 11 a.m. to 4 p.m.; Sunday, August 23, 10 a.m. to 4 p.m.; Monday, August 24 onwards, 9 a.m. to 6 p.m. The registration fee will be £4 sterling, and concessionary fees are charged to those who take part for less than the full week.

METHYLPENTYNOL

A good many years have passed since a new kind of hypnotic has been discovered, and we have grown accustomed to the almost exclusive use of the barbiturates in one form or another. About two years ago Margolin and his colleagues[1] described the hypnotic properties of 3-methyl-pentyne-ol-3. The structure of this substance can be regarded as derived from that of methyl alcohol, CH_3OH, by substituting for the three hydrogen atoms (1) $-C_2H_5$, (2) $-CH_3$, and (3) $-C_2H$, respectively, the last substituent being the group remaining when one hydrogen atom is removed from acetylene, so that it can be written $-C\equiv CH$. Methylpentynol, as it is called (or methylparafynol), is unlike methyl alcohol in that it does not cause intoxication, but when administered to animals or man it sends them to sleep. It can be given by mouth. In addition it has the very important advantage that it is broken down in the body with fair speed. The safety of a hypnotic depends on the rate of its removal or breakdown, and when methylpentynol was given to dogs in amounts of 200 mg./kg. less than 5% was excreted during 24 hours, and none could be detected in the blood after two hours.

Hirsh and Orsinger[2] have studied the hypnotic action in 276 patients of ages from 20 to 83 suffering from various diseases, and found that when 500 mg. was given 93% fell asleep in one hour and slept for five hours or more. Only 5 out of the 276 noticed any after-effects.

1 *Science*, 1951, **114**, 384.
2 *Amer. Practit. (Philad.)*, 1952, **3**, 23.
3 Malone, H. J., Klimkiewicz, G. R., and Gribetz, H. J., *J. Pediat.*, 1952, **41**, 153.
4 Chevally, J., *et al.*, *N.Y. St. J. Med.*, 1952, **52**, 572.
5 Allen, A. W., and Krongold, D. D., *Quart. Bull. Sea View Hosp.*, 1951 **12**, 61.

Several other clinical reports have been published[3 4 5] in which similar results have been described. In all the clinical trials sleep was induced in a very high percentage of subjects, with no hangover on awakening and no nausea or other reactions. In one case the drug was taken daily for six months. Dogs and rats have been given amounts equivalent to 70 times the therapeutic dose, and no gross pathological changes were found and no abnormalities of the blood, of renal function, or of blood sugar. There appear to be no contraindications to the use of methylpentynol. It has been given safely to patients with hypertension, arteriosclerosis, portal cirrhosis, and diabetes. Children in hospital who experienced long periods of wakefulness and restlessness before sleep were able to sleep more quickly when given 150 mg. of methylpentynol, and were not drowsy when they awoke. In some cases sleep was permanently improved when the drug was given for a month and then stopped.

An overdose of methylpentynol causes deep sleep from which the subject can be roused by the injection of caffeine. The drug is said to have no depressant action on heart and respiration and no anaesthetic or analgesic action. For this reason it is less effective when sleeplessness is due to pain.

All the published accounts suggest that a useful new means of dealing with insomnia has been discovered. But a cautious attitude about the safety of methylpentynol must be maintained until it has been more widely used, for most new drugs pass through a phase in which they are esteemed too highly. A substance of this kind, related to alcohol, will almost certainly have depressant effects on the liver, on the heart, and on the respiration, even if these are slight, and no responsible person should suggest at this stage that it is completely harmless.

BIOLOGICAL SYNTHESIS OF VITAMIN C

An important advance in our knowledge of how plants make vitamin C has recently been achieved at Cambridge by Mapson and his colleagues. Vitamin C, or ascorbic acid, is closely related to the hexose sugars, of which glucose is the most familiar. But whereas glucose has a D configuration according to a scheme based on the structural formula rather than on the actual optical rotation, the natural form of ascorbic acid has an L configuration. In the manufacture of synthetic vitamin C, therefore, glucose cannot be used as the starting point. The chemist has to turn to sorbose, a less readily available hexose having an L configuration.

But twenty years ago Ray[1] showed clearly that the plant is less particular in its choice of starting material for synthesizing the vitamin. When excised pea embryos were nourished on media containing various sugars, glucose was found to be highly effective in increasing synthesis. Since ascorbic acid is formed by all plant tissues, and not only in those rare instances in which L sugars predominate, Ray's observations were perhaps only to be expected. The subtle mechanisms of the plant cell can obviously induce structural changes in the hexose molecule in ways which cannot yet be imitated by the organic chemist.

Until recently we were not only unable to imitate the plant's mechanism, but had no reasonable theory about the sequence of the reactions leading to the production of the vitamin from glucose. Thus it was thought possible at one time that D-hexoses, such as glucose or galactose, might be split up into trioses, which could then be recombined in an L configuration. But experiments with the rat, an animal which resembles the plant in being able to synthesize ascorbic acid, failed to support this view. When glucose uniformly labelled with radioactive carbon atoms was administered, the ascorbic acid which was produced from it was also found to be uniformly labelled. This would be an improbable finding if the glucose molecule had been split in half, since most of the radioactive triose would presumably have recombined with non-radioactive trioses formed in the normal course of metabolism.

The evolution by Isherwood, Chen, and Mapson[2] of an alternative theory which seems completely to fit the facts must therefore be counted an outstanding scientific advance. These workers took their clue from the well-known observation that when animals are dosed with hypnotic drugs, such as chlorbutanol, the production of glucuronic acid, which is used for detoxication, is accompanied by a large increase in the production of ascorbic acid. Might this not mean that glucuronic acid is an intermediate step in the production of ascorbic acid from D-hexoses?

Intensive chemical studies in which various hexoses and derivatives of glucuronic acid were tested as sources of L-ascorbic acid confirmed this hypothesis, and gave an ingenious explanation of the reversal between the D and L configurations. Let us picture the glucose molecule as having a hydroxyl (reduced) group at one end and an aldehyde (oxidized) group at the other. Further oxidation of the aldehyde group to form the carboxyl group of glucuronic acid would leave the configuration in the D form, and attempts to synthesize ascorbic acid would inevitably end with the D isomer, which has very little biological activity. But if the oxidation to carboxyl occurs at the alcohol end of the molecule, and the aldehyde group is later reduced, the configuration of the molecule is effectively turned upside down. Processes directed towards the formation of the ascorbic acid must now produce the natural L variety.

According to Isherwood, Chen, and Mapson the steps along the route of synthesis in the plant or animal are D-glucose, D-glucurono-γ-lactone, L-gulono-γ-lactone, and L-ascorbic acid. With galactose the corresponding steps are D-galactose, D-galacturonic methyl ester, L-galactono-γ-lactone, and L-ascorbic acid. L-Galactono-γ-lactone is more efficient than L-gulono-γ-lactone in promoting the synthesis of ascorbic acid in plants, but both are equally effective in animals. Experiments on

[1] Ray, S. N., *Biochem. J.*, 1934, **28**, 996
[2] Isherwood, F. A., Chen, Y. T., and Mapson, L. W., *Nature (Lond.)*, 1953, **171**, 348.
[3] Mapson, L. W., *Proc. Nutr. Soc.*, in the press.

the synthesis of vitamin C by enzyme systems *in vitro* are proceeding, and successful preliminary experiments are, we understand, soon to be published.[3] The enzyme necessary for the conversion of the γ-lactone to ascorbic acid is present in the mitochondria of plant cells.

MORPHINE AND ALCOHOL

A few weeks ago we discussed the synergistic action of alcohol and barbiturates taken together, and suggested that drivers of cars would be very unwise to mix their drugs in this way.[1] Two recent papers from Professor K. O. Moeller,[2 3] of Copenhagen, contain some details about the effects of morphine on patients who had fairly high concentrations of alcohol in their blood, and he reports seven deaths. The alcohol concentration in the blood of these patients was from 0.18 to 0.27%, far lower than the amount usually regarded as lethal (0.4 to 0.5%). One patient was a woman with cholelithiasis. She was strongly addicted to alcohol, and had already consumed a large quantity when she went to her doctor for an injection to relieve her pain. As he was not at home at the time she persuaded the doctor's wife to give her an injection of 20 mg. (⅓ gr.) of morphine. Two hours later the patient was found unconscious at home and she died shortly afterwards. At necropsy gall-stones were found in the gall-bladder, morphine in the liver and urine, and alcohol in the blood in a concentration of 0.2%. In a second fatal case morphine was given for biliary colic and in a third for renal colic (stones were present in both). In the remaining four cases morphine or morphine and scopolamine was given to quieten restless or violent alcoholics—the dose of morphine varying from 15 mg. (¼ gr.) to 26 mg. (⅜ gr.) —and in addition two of the patients were also given an intravenous injection of a barbiturate compound. All died from one and a half to five hours after the administration of morphine. In healthy individuals the lethal dose of morphine is as high as 100 mg. (1½ gr.) by subcutaneous injection, and, since the concentration of alcohol in the blood of all these patients did not approach the lethal amount, Moeller concludes that morphine acts synergistically with alcohol. Thus the administration of morphine to patients under the influence of alcohol may have serious consequences.

CARE OF AGED IN SCOTLAND

The study of how best to care for old people is in no danger of becoming one of the neglected backwaters of medicine. Now a new report[4] from Scotland adds some sound and kindly advice on what is already a considerable problem. Between 1921 and 1947 the number of people of pensionable age in Scotland rose from 377,000 to 629,000. By 1969 they are expected to number 858,000, or 15.5% of the population, as compared with 7.7% in 1921. The proportion of elderly people varies in different areas, in 1947 ranging from 25% in the north to 10% in the Lanarkshire burghs. This is no doubt one of the consequences of industrialization, for the young men are tempted to seek their living near the city lights. The old people are left behind, and families are neither large enough nowadays to care for the elderly members easily nor so dutiful as to make the often considerable sacrifice that was expected in former times.

The ideal that this report advocates is "to have healthy people living their own lives in their own homes, and to postpone senescence as long as possible." Much can be done, the report adds, and perhaps the most pressing of the needs whose fulfilment it advocates is the provision of suitable houses and, where necessary, domestic help. In the long run this is probably of much more importance to the wellbeing of the old than anything the health services can offer, and it is a matter for regret that the authors of the report found a "great lack of information and knowledge" here. They were right to point out also—though without the emphasis it deserves—that a happy old age is something that must be prepared for. It is not so much a question of cheap tobacco and Windsor chairs and T.V. sets as the consequence of a youth ill or well spent. Whether the Welfare State, in partly relieving many people of the need to save up for old age, will also diminish their capacity to prepare mentally for it is a matter for speculation. But at any rate the report does make the point that old people's interests must be kept up, hobbies encouraged, and loneliness dispelled.

For people who cannot, even with help, manage their own lives, some kind of hostel care is necessary—and much more of it than exists at present. The committee finds that about 10,000 places are available but that at least 17,000 are needed. Nor is their provision a matter only of affording the most suitable accommodation: the scarcity of hostel places is uneconomic, for 35 old people in a hostel can be looked after by a staff of 7 or 8, in a general hospital by about 20, in a long-stay annexe by 13 or 14, and in their own homes by about 12 full-time home helps. There are clearly strong arguments here for including more hostels in the current building programmes.

The report is rightly emphatic about the need to restrict hospital admissions of elderly people to those who require investigations or treatment best undertaken in hospital. And the corollary is no less important—namely, that the patient should be discharged when the investigation or treatment comes to an end. Unfortunately many circumstances compel hospitals to depart from these ideals, one of the commonest being that there is no home to which the patient can be discharged. While this again is a problem that is perhaps more social than strictly medical, the report has some valuable suggestions on the part that efficient aftercare services could play in helping the old person get back to health outside hospital. But until long-term measures get going the elderly are bound to make considerable demands on hospital beds, and all who have the care of them will especially welcome the committee's plea for more field research into the best means of helping them.

[1] *British Medical Journal*, 1953, 1, 1269.
[2] *T. norske Laegeforen.*, 1953, 73, 1.
[3] *Ugeskr. Laeg.*, 1952, 114, 1785.

[4] *The Ageing Population*. Department of Health for Scotland. H.M.S.O., 6d. Prepared by a subcommittee of the Standing Medical Advisory Committee. Members: Dr. W. G. Clark (chairman), Dr. A. D. Briggs, Dr Mary Esslemont, and Professor I. G. W. Hill.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

SUBACUTE BACTERIAL ENDOCARDITIS

BY

RONALD V. CHRISTIE, M.D., F.R.C.P.

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The effective use of antibiotics has not only changed the prognosis and clinical course of subacute bacterial endocarditis but has entirely altered the emphasis on early diagnosis. Ten years ago the diagnosis was seldom made until the disease was well established, while today any patient with a heart murmur and unexplained fever should be suspect. In my own wards patients suffering from rheumatic fever, cystitis, glandular fever, virus pneumonia, carcinoma of the stomach, periarteritis nodosa, haemolytic anaemia, and perianal abscess have been admitted with the diagnosis of subacute bacterial endocarditis, and in each case, although the initial diagnosis was shown to be wrong, the admission of the patient to hospital should be taken as evidence of good judgment and efficiency on the part of the general practitioner involved. Early diagnosis is of great importance to the patient, therefore a full investigation is indicated when subacute bacterial endocarditis is first suspected.

Early Diagnosis

It is unfortunate that the early clinical manifestations are not only variable but often vague and ill defined. Fever is probably the most reliable early sign, but the degree of malaise with which it is associated is often so slight that it may pass unnoticed. The first complaint is usually of fatigue, loss of appetite, and sometimes pains in the joints. The patient may feel chilly and slightly feverish, and the temperature is found to be raised. If the patient is examined at this stage some of the physical signs of the disease such as splenic enlargement, petechiae, or embolic phenomena may be found, but often these are absent and the diagnosis can be established only by blood culture. Less frequently the disease remains unsuspected until the sudden onset of rigors and fever or of embolism and infarction.

Early diagnosis is now important, since delay in treatment undoubtedly diminishes the chances of survival, not because the infection is less readily controlled but because damage to the heart is both progressive and dangerous. Any patient with valvular or congenital heart disease who has unexplained fever should be suspect, and it follows that in the differential diagnosis all conditions which give rise to prolonged fever have to be considered, particularly those associated with splenic enlargement. Urinary infection is a common source of error, and tuberculosis and typhoid, glandular, and other fevers may have to be excluded.

The most difficult disease to distinguish from subacute bacterial endocarditis is rheumatic fever, a difficulty which was emphasized by Horder over 40 years ago. "It is probable that all the symptoms and signs of infective endocarditis may be met with in rheumatic fever, save the isolation of micro-organisms from the blood. Recurring attacks of subacute rheumatism in patients who have previously developed valvular disease often give rise to considerable anxiety on account of the similarity which they bear to the symptoms of infection of the endocardium." It is now much more important than it was to distinguish between these two diseases, but unfortunately there has been no corresponding improvement in diagnostic methods during the past 40 years. Even if blood cultures are repeatedly negative the diagnosis may remain in doubt, and therapeutic tests, first with salicylates and then with penicillin, may have to be resorted to. The response to cortisone should never be used as a guide, since this may be disastrous in patients with subacute bacterial endocarditis.

Treatment

A unique feature of this disease is its resistance to treatment, although the infecting organism, which is usually a streptococcus viridans, may be sensitive to penicillin and to a variety of other chemotherapeutic agents. Large doses of penicillin are now recommended, and, although accurate figures are not yet available, it seems probable that the infection can be controlled in 95% or more of the cases. When the organism is not more than twice as resistant to penicillin as the standard Oxford staphylococcus, 2,000,000 units a day for four to six weeks will almost always be effective. In about 10% of cases the resistance of the organism is approximately four times that of the Oxford staphylococcus, and in these the daily dose should be increased to about 4,000,000 units. In about 5% of cases the resistance of the organism is more than eight times that of the Oxford staphylococcus, and under these circumstances the system of dosage to be adopted should be decided only after careful consideration of each individual case.

It is with this group of patients that disappointing results have been obtained. Information is as yet inadequate on the system of dosage which should be adopted in the treatment of these resistant cases, but in general it is true that the best results are obtained when the daily dose, if given by continuous infusion, would maintain a concentration in the blood which is about 50 or 100 times as great as the concentration required to kill cultures of the organism. In some patients very large amounts of penicillin may be sufficient, either when given alone or when given with some substance such as probenicid which delays the excretion of penicillin. As much as 40,000,000 units a day may be required, but when this degree of resistance is encountered the use of other antibiotics should always be considered, and it is in making this selection that mistakes are often made.

When antibiotics other than penicillin are used it should be borne in mind that bacteriostatic agents such as aureomycin and terramycin are seldom effective even when laboratory investigations indicate that the organism is highly sensitive. The practice of giving aureomycin because the laboratory report seems favourable and because the patient does not appear to be responding to penicillin should be condemned, since it seldom succeeds and usually only leads to delay in effective treatment. A more profitable line of approach is a combination of penicillin with streptomycin, which is also bactericidal, but it should be emphasized that combined antibiotics should be used only under close laboratory supervision. The interaction of antibiotics is a matter of great complexity, and the laboratory supervision of cases which are resistant to treatment with penicillin demands a high degree of skill and specialized knowledge.

For obvious reasons the patient should be confined to bed and the general principles involved in the treatment of any prolonged febrile illness should be applied. Anaemia should be given treatment appropriate to its severity, and it is important that an adequate state of nutrition should be maintained. Foci of infection should be searched for, and dental sepsis should if possible be eradicated while the patient is being treated with penicillin.

Response to Treatment.—The blood culture usually becomes sterile within a few days of the beginning of

treatment, but not infrequently fever persists longer, although it usually falls within a week. The danger of infarction and other embolic phenomena remains throughout treatment and convalescence, but in lessening degree. The spleen diminishes in size, often quite rapidly. In contrast, haematuria may persist long into convalescence. The erythrocyte sedimentation rate may remain high during treatment, but falls slowly during convalescence. In the absence of complications such as heart failure or major emboli it is usual to allow patients to sit in a chair for a week after the cessation of treatment, and then to encourage an increase in activity according to the patient's capacity.

Relapses, Prophylaxis, and Prognosis

Relapses.—These seldom occur more than a month after treatment, but a slight risk, amounting to about 2% of patients per annum, of relapse or reinfection remains. The treatment of patients who fail to respond to the usual dosage presents a special and difficult problem. A larger dose should be given, probably at least 5,000,000 units a day for a period of six to eight weeks, but, as already emphasized, the system of dosage should be carefully regulated according to the sensitivity of the infecting organism.

Prophylaxis.—Dental extraction and removal of other foci of infection have long been regarded as precipitating factors in this disease. In patients with rheumatic endocarditis or congenital heart disease a prophylactic course of penicillin for these minor operations should be insisted upon. A dosage of 500,000 units daily for three days is usually recommended, the first dose being given an hour or two before the operation. It is perhaps not generally realized that this system of dosage, which is the one generally used in prophylaxis, is based not on clinical trials but on an intelligent guess made many years ago when penicillin was in short supply.

Prognosis.—Death from heart failure is now a much greater hazard to the patient than the risk of failure to respond to penicillin. About a third of the patients who are apparently cured die in heart failure within two years of treatment with penicillin, and the outlook is particularly gloomy in those who have evidence of heart failure when treatment is started. If heart failure is severe the patient rarely survives more than a few months, and even if it is slight the chances against survival for more than two years are about four to one. Other adverse factors in prognosis are delay in treatment and relative insensitivity of the infecting organism to penicillin.

Refresher Course Book.—The first collection of articles of this series (fully revised) are available as a book containing 55 chapters, price 25s. Copies can be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

Nova et Vetera

THE DISCOVERY OF INSULIN

The Nobel Prize was awarded in 1923 to Banting and Macleod "for the discovery of insulin." Macleod's contribution to this dramatic discovery has been for long disputed. It is widely thought to have been both considerable and direct, and nearly 20 years later, in 1941, the *British Medical Journal* obituary notice on Sir Frederick Banting referred to "experiments in collaboration with the late Professor J. J. R. Macleod and Dr. C. H. Best which led to the discovery of insulin." Macleod's close participation in the research would not have been surprising, for the absorbing interest of his academic life was the metabolism of carbohydrates. His first papers on experimental glycosuria were published in 1905, and a series of 12 papers under the general title of "Studies in Experimental Glycosuria" was published in the *American Journal of Physiology* between 1907 and 1917 in addition to a series of 18 papers between 1908 and 1921 dealing with other aspects of carbohydrate metabolism.

Yet his inclusion in the Nobel Prize award led to bitter criticism of the prize-jury's decision. It was alleged that Macleod had been away from Toronto when the decisive experiment was made, and that, although he had put the facilities of his laboratory at Banting's disposal, he had had no part either in the formulation of the hypothesis on which the discovery was based or in any of the experimental investigations by which insulin was isolated and evaluated as a therapeutic agent. Best, who was Banting's close and acknowledged collaborator, was not given a share in the honour. According to Göran Liljestrand (1951), Banting expressed his dissatisfaction by sharing his half of the prize with Best, whereupon Macleod gave a corresponding part of his to J. B. Collip, who had participated with him in the purification and standardization of insulin.

Some Simple Facts

Nearly 30 years after the event we can now read Best's version (1952) of the early days, given as his corrective to "a few interesting statements about the early development of insulin which I completely fail to recognize." In the Banting Memorial Lecture for 1952 he writes:

"The facts are simple and straightforward. The young surgeon formulated an hypothesis which was vital to his initiation of the work and it thus completely fulfilled its function. He obtained permission to explore this hypothesis in the Physiological Laboratory of his Alma Mater and he received some excellent general advice from the Head of the Department. The second working hypothesis was that an internal secretion of the pancreas existed and that it could be captured. This one Banting and I shared, and in its exploration we invested our time and energy. We formed a partnership which was based on the new knowledge and experience which we gained together. We had no stipends, but the facilities of Professor Macleod's deserted department were at our disposal. *We worked completely alone during the four summer months of 1921 without any verbal or written advice from any senior investigator and until well after the salient facts, consistent dramatic lowering of blood and urinary sugars and complete recovery of our moribund depancreatized dogs, had been repeatedly demonstrated.*" (There are no italics in the original.)

"Banting and I presented our work to the Medical Faculty at a departmental seminar in the autumn of 1921, and our findings were later published in two papers under our names in the *Journal of Laboratory and Clinical Medicine*. These papers give the first detailed account of our isolation of insulin. We were given an impression that a member's name was necessary for the acceptance of a paper to be read at the meeting of the American Physiological Society, and for this reason Professor Macleod's was added to the preliminary paper presented in December, 1921. Banting and I always hoped that our article on 'The Internal Secretion of the Pancreas,' which appeared in the February, 1922, issue of the *Journal of Laboratory and Clinical Medicine* and which we wrote for and presented to our Medical Faculty on November 14, 1921, would be universally accepted for what it in fact was, the original record of our work. The paper which bore, in addition, the name of the Head of the Department was a summary of the longer one. We prepared it later, but it appeared in print first."

Another commonly held misconception is also dispelled by Best—namely, that he was a medical student when he volunteered to work with Banting. He was, in fact, after five years of university study (and a year in the Canadian Army) a very recent graduate in the arts course of physiology and biochemistry. For family reasons he was particularly interested in diabetes and had been a part-time research worker on this subject and a demonstrator in physiology to medical students during 1920–1. He registered for an M.A. in physiology during the year that he and Banting worked together and was admitted to the degree in June, 1922. It was not until September, 1922, 16 months after the joint work on insulin had begun, that he decided to proceed to an M.D. and registered as a medical student in the University of Toronto.

HENRY COHEN.

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Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

The Pain of Transurethral Manipulations

SIR,—As a general practitioner I cannot listen unmoved to my patients' accounts of how they have suffered during their in-patient treatment for genito-urinary complaints. During the past few years one after the other has told me of the agony he has suffered during cystoscopy and ureteric catheterization, and particularly during such transurethral manipulations as are required to treat the complications of prostatectomy whichever route is employed. It appears that some attempt is made at anaesthetizing the urethral mucosa with a surface anaesthetic, but the preoperative injections do little to support them during the ensuing ordeal.

These men tell me that they have endured as much as they can bear, and in two cases, where repeated manipulations were required for treatment of neoplasm, the patients discharged themselves because they were not brave enough to endure any more. These patients were not neurotics, and I hear no complaints from those who have undergone other forms of surgical treatment. Nor have all these patients attended the same hospital, but four different centres, so I assume that the technique differs little from place to place.

Are anaesthetists so few that none can be spared for "minor" genito-urinary sessions? Or do surgeons hesitate to employ them for "minor" procedures because the complexity of modern anaesthetics tends to reduce the operations to a mere incident in the induction of the anaesthesia? At all events it seems that the demon pain has been evicted from nearly every corner of surgery except from the cystoscope and other things which are pushed up the male urethra. I am aware that genito-urinary surgeons are not by nature callous, but by long practice they have come to countenance the patients' reactions to urethral instrumentation as routine. The consolation that "it will soon be over" and "it has *got* to be done" does little to dull the pain of a large-size operating cystoscope turning through 360 degrees in the urethra—likewise the bladder washout via the urethra to control post-operative haemorrhage—for by then the spark of human vitality has grown very dim and the patient has literally reached the limit of endurance.—I am, etc.,

Sheffield. E. C. ATKINSON.

Comfort in Callipers

SIR,—Dr. H. L. Rogerson (*Journal*, August 8, p. 337) has, I am afraid, done nothing to improve the design of the walking-calliper. What he has produced is not a calliper but a walking-splint for the lower extremity, the design of which is rooted in greater antiquity than the "antiquated calliper" about which he complains. This is not to say that his appliance is not an excellent one for his own particular case and illustrates the virtues of what one may call bespoke craftsmanship. The appliance is an expensive one to make, and, though it may stand up to Dr. Rogerson's personal needs, would not be suitable for everyday use by the majority of patients. For nine out of ten cases of poliomyelitis with the amount of paresis which he described (especially those who are young, active, and often heavy) it would be mechanically unsound.

The principle of the long outside iron fitted to a pelvic band was in use in the early nineteenth century. It was discussed and discarded by H. O. Thomas for the purposes for which he designed the calliper. The self-locking and quick-release knee hinge, the posteriorly placed knee hinge, and the eccentric articulation are all well known to surgical appliance makers; there is nothing new in that. The use of "duralumin" is of dubious advantage, for it has not, size for size, the strength of steel, it cannot readily be forged, and in jointed parts the friction surfaces must be faced with steel. A well-forged steel appliance is little, if any, heavier than duralumin and is stronger. Certainly at the hip the need for strength is very great.

From hard experience one must say that in splint design "there is nothing new under the sun." Dr. Rogerson has, however, emphasized the need to provide long-term appliances for poliomyelitis which are made by individual craftsmanship for the particular problem. Mass production cannot solve this problem.—I am, etc.,

Exeter. NORMAN CAPENER.

Fog Control in the Home

SIR,—In view of the great increase in sickness and deaths from pulmonary disorders attributable to the poisonous composition and long duration of the London fog of December 5–9, 1952, and the possible recurrence of that disaster, it is essential that any valuable lessons to be learnt from that experience should not be lost sight of.

In this connexion I beg to draw attention to certain ready and practicable measures which the householder can take to prevent the gross penetration of fog into living-rooms and bedrooms, as illustrated by the case of a lady aged about 75 living in London, who invariably suffers from bronchitis during the winter. Some years ago she had the open fireplace in her bedroom sealed off and used an electric radiator for heating the room. Normally she keeps the windows open, but during the intense fog of December, 1952, they were closed and the room, in which she was confined to bed, was practically free from fog during the worst period. I think she owes her survival to this fact.

Based on this experience, I do feel that in the event of a recurrence of dense fog the following action should be taken in houses supplied with electricity. No open fires or gas fires should be lit in living-rooms or bedrooms, as the room air passing up the chimney causes fog-laden air to be drawn into the room from outside. Windows should be kept closed and fireplaces or chimney flues sealed off, as an open flue causes a good deal of ventilation even though the fire is not lit. Electric radiators should be used if heating is required in the room, but less heat will be needed, as the ventilation is reduced. Provided flueless gas heaters are not used in small rooms, it might be desirable for air-bricks to be sealed up during the fog and to reopen them and unseal the fireplaces in other rooms as soon as the fog has abated.

If prompt action is taken to carry out the above recommendations, not only will the gross penetration of fog into rooms be prevented but its entry into the house as a whole will be lessened. These measures are calculated to be of particular benefit to persons with respiratory disabilities whose distress is aggravated by breathing fog-laden air.

Finally, Sir, it may be worth while recalling that the A.R.P. sealing of rooms to prevent the entry of poisonous gas was carried out by countless householders in the early days of the war. It would be gratifying if that experience finds application in ordinary times pending the hoped-for solution of the difficult problem of atmospheric pollution.—I am, etc.,

London, W.C.1. GUY P. CROWDEN.

Chronic Bronchitis

SIR,—The annotation under the above heading (*Journal*, August 1, p. 268) is very timely. It points out the extreme gravity of the condition and draws attention to the economic loss we suffer from a too facile attitude to coughing. I believe we shall not progress in prevention of this and other chest diseases until we regard a persistent cough as seriously as persistent vomiting. The two symptoms have similar causes, infection and local irritation being the most prominent. In 1950, the last year for which figures are available, 16,500,000 working days were lost in England and Wales from bronchitis. Your contributors are too pessimistic when they conclude that a logically planned attack is not yet possible. Most of the factors are known—they are: (*a*) recurrent infection related particularly to overcrowding at home, at school, and at work; (*b*) atmospheric

pollution; (*c*) inhalation of dust and fumes at work; and (*d*) smoking, especially cigarettes.

As a profession we can do much more about each of these problems than we do at present. Our views on the lives of people in overcrowded areas have not been expressed sufficiently forcibly. In the Gorbals district of Glasgow 296 people live on each acre of ground. Cattle could not exist in such numbers. The incidence of tuberculosis and respiratory disease is closely related to this factor. The conditions in many urban and rural schools prevent children remaining well. Those responsible for the health of school-children should press for more healthy provision for scholars. Early and continued attention should be given to each attack of respiratory infection, and more seaside and country convalescent homes should be available for use by the general practitioner. It is absurd that a patient must be referred to hospital before convalescence can be arranged.

The overwhelming importance of atmospheric pollution in relation to respiratory disease was demonstrated by the great London fog of December, 1952. 6,000 people died as the direct result of this, while hundreds of thousands had their bronchitis exacerbated and their lives shortened. At the same time some of the finest cattle from the countryside were unable to live in our vitiated air and died of bronchitis and acute emphysema during a cattle show. No more scientifically controlled experiment could have been devised and yet it seems that little will be done. Eight months after the event a committee is set up by the Government to study the problem. In the past this has so frequently been a device for ensuring no action was taken that one fears this may be intended again. As a profession I think we should be active in smoke abatement both at home and nationally. Life could be much more pleasant and healthier, despite our damp climate. The conditions in factory, foundry, and mine leave much to be desired in most areas. Chronic pulmonary cripples are being produced each year by needless dust and fumes. The workers of the country must breathe pure air.

Finally, the harm done by smoking must be appreciated. No person who has smoked cigarettes for 20 years or more fails to cough—and many cough persistently each morning. Few will admit this because of a desire to continue the addiction. In practice more than 80% of bronchitics are heavy smokers. We should set them an example by not smoking ourselves and then assure them that unless they give up smoking no adequate relief from coughing can be expected.

The air we breathe is as important as the water we drink. It must be uninfected and unpolluted. A sanitary revolution commencing 100 years ago has done much to eliminate water-borne disease. We should work for the elimination of bronchitis and other air-borne diseases.—I am, etc.,

London, N.W.10. H. JOULES.

Breast-feeding in Oxford

SIR,—I was very interested in the paper by Drs. Alice Stewart and Celia Westropp on breast-feeding (*Journal*, August 8, p. 305). I feel, however, although I am in no sense a statistician, that the conclusions are fallacious. The following are some of the criticisms which seem to me to invalidate the conclusions.

The children studied were selected. The writers state that "the enrolment procedure effectively excluded babies who were seriously ill at or before this age (2 months)." What proportion of the babies excluded were breast-fed at 2 months? It is very likely that a large proportion were bottle-fed. In that case an unduly large proportion of babies who had been ill would be excluded from the artificially fed group, and so the entire results would be invalidated.

There is no mention as to how and by whom the various observations were made. Were all the babies examined by the same person, and did that person know to which group the babies belonged? If she did, the element of bias was not eliminated. This might well be important, for several of the features studied were matters of opinion and interpretation. How, for instance, was the "closure of the fontanelle" assessed? If it was assessed by palpation, then it was a matter of opinion whether it was closed or not. Bias might well affect that opinion.

The writers say that "at the age of 1 year the babies who were bottle-fed from the beginning . . . showed signs of being slightly more mature." I can find no evidence for that statement. It is not clear what is meant by "more mature," but, if it refers to the radiological data, the "closure of the fontanelle," and the "crawling and walking," then I cannot see how that conclusion was reached. They give figures for the appearance of the distal radial epiphysis: unless my deductions from their Table are incorrect, 61% of those weaned at or after the fourth month had the distal radial epiphysis, as compared with exactly the same proportion, 61%, of those weaned earlier. Their Table shows that there were exactly the same number of carpal bones (2.24) per radiograph per child in the two feeding groups, group 1 (babies weaned in the first month) and group 4 (weaned after the fifth month). As for the closure of the fontanelle, the differences between the various groups are not statistically significant (unless my mathematics are wrong), neither is there even a constant trend in the Table: for 41.7% of those in group 2 (babies weaned in the second or third months) and 31.1% in group 3 had a "closed fontanelle" at 12 months as compared with 30.3% in group 1 (those weaned in the first month).

As for the "milestones," walking and crawling, unfortunately these are not defined. Does "walking" mean walking with two hands held, one hand held, or without support? And was it assessed by the mother or doctor? However, taking the figures as they are given, once more there is no evidence to support the statements made: 63% of the babies in groups 3 and 4 were crawling at 10 months, as compared with 64% in groups 1 and 2; 71.7% of those in group 3 were crawling at 10 months, as compared with 61.8% of those in group 1. As for "walking," the difference between groups 1 and 4 is not of statistical significance. I do not think that many will accept the statement that "at 14 months the babies who were breast-fed longest were very slightly 'less mobile' than the others." It is interesting to note that the average number of teeth in group 4 at 12 months was 6.04, as compared with 6.82 in group 1. But in what way does it matter?

In the section on the incidence of infection, I am not able to follow all the statistical arguments. But what is the meaning of the statement: "In the case of head colds it was often impossible to identify the precise mode of feeding at the time of the illness"? Do the data on the method of feeding depend on the mother's memory of what she did some months back? Having shown that the incidence of colds is greater, as is well known, in households in which there are schoolchildren, the writers do not say whether the incidence of households with schoolchildren is the same in the four feeding groups. If it were different, it would alter the incidence of infections in the various groups.

The writers discuss the fact that the bottle-fed babies weighed slightly more at 12 months than the breast-fed babies, and say: "We are therefore driven to the conclusion that, in spite of continuous medical supervision, minor degrees of underfeeding among the breast-fed babies had occurred and had been overlooked." Surely that argument is fallacious. Because one child weighs less than another at the same age it does not mean that he is underfed. Babies who are weaned early might well be given rather a lot of starchy foods, which would increase the weight. But surely there is no evidence to suggest that such babies are better because they are bigger.

There are other points in the paper which cast doubt on the validity of the results, but space will not permit of their consideration here.—I am, etc.,

Sheffield. R. S. ILLINGWORTH.

SIR,—I found the Oxford breast-feeding survey by Drs. Alice Stewart and Celia Westropp (*Journal*, August 8, p. 305) very interesting, particularly as the findings were in rather striking contrast to a small survey I did in Bristol in 1942–3. In this survey, for which statistical details are, unfortunately, not available, 1,000 consecutive cases were studied. They were studied in four groups: (1) 1–6 months, subdivided into 1–3 months; (2) 6 months–1 year; (3) 1 year–18 months; (4) 18 months–2 years. They were investigated for colds, tonsillitis, otitis media, gastro-enteritis, broncho-pneumonia, and skin infections.

My figures showed that upper respiratory infections were definitely more common in the bottle-fed children in group 1. Gastro-enteritis was slightly more common and more severe in the bottle-feds up to 18 months. The incidence of bronchopneumonia in groups 3 and 4 was about equal, but was more severe in the bottle-fed babies. Skin infections, particularly eczema, were not frequent in bottle-feds in each age group.

The bottle-fed infants weighed more than the breast-fed, but maturity was not assessed, except in regard to crawling and walking. The breast-fed babies were, in this series, the more mobile—possibly, I thought, owing to being lighter in weight.—I am, etc.,

Farnham Royal, Bucks. MARY HERFORD.

Clinical Research in the N.H.S.

SIR,—I would like to support the letter from Dr. G. I. Watson (*Journal*, August 1, p. 286).

"Systematic investigations undertaken deliberately and often over long periods" are just the sort of investigations which general practitioners, either singly or in groups, would be most likely to undertake successfully. The more intensive type of investigation is particularly difficult for them, except as members of a team led by whole-time research workers.

I am glad that Dr. Watson has pointed out this unfortunate misconception in the White Paper.—I am, etc.,

Cirencester. R. E. HOPE SIMPSON.

SIR,—I have had some experience of clinical research supplemented by experimental research. I have come to the conclusion that clinicians, which includes general practitioners, should be given an opportunity of doing part-time research of not less than two sessions per week with generous remuneration. Clinical research should not be restricted to those of registrar status, and the staff of hospitals should be encouraged to do this part-time work.

A niche in a research laboratory, with the services of a trained technician, should be provided, preferably at a research institute attached to a teaching hospital or to a university, where the advice and help of the departments of anatomy, physiology, pathology, radiology, and physics, etc., are available. The co-operation and support of one's colleagues and a supply of clinical material are essential.

Animal experiments require a team of an experienced experimenter with a licence, a trained technician, and an observer (a clinician or research worker), and in some experiments a physicist is desirable. Animal experiments may last five or more hours.

A clinician who has retired from his hospital appointment is well able to do clinical research in his spare time. He will find it interesting and he will be able to contribute something useful to medicine.

I could enlarge on this theme and give more details, but space will not permit.—I am, etc.,

London, W.1. E. D. D. DAVIS.

Indigestion in Childhood

SIR,—As a general practitioner I have read Professor Norman B. Capon's Refresher Course article on indigestion in childhood (*Journal*, July 25, p. 197) with special interest, for there are few patients who cause more trouble to parents and G.P.s than the child with indigestion or who "won't eat." In some ways the G.P. who follows these cases from babyhood to maturity, and sometimes from generation to generation, is more fortunately placed to observe them even than the paediatrician; so continuous practice in a small town for some 30 years must be my defence for making some contentious observations on the paper of an expert that I have read with pleasure, particularly his remarks on the general management of these cases.

The first comment I would make, which will doubtless be met with the criticism that I have a one-track mind, is that I am sorry Professor Capon only mentioned appendicitis in connexion with acute indigestion. In my experience it is a common cause of the chronic variety also. I know this is often disputed, but as I was, I believe, the first person in this country to postulate from clinical examination the existence of "measles appendix,"[1] which was shortly afterwards described by a German pathologist. I have at least some claim to be able to recognize a pathological appendix when I meet one. Incidentally, the histological features of the measles appendix are so characteristic that some years later a surgeon in America removed an appendix, sent it down to the pathologist, and received the diagnosis of measles before the rash appeared, which it duly did.

In these childish cases the children seldom complain of abdominal pain unless the appendix is lying just below the abdominal wall. A more common complaint is a "stitch" in the right leg presumably due to irritation of the ileo-psoas, on or near which the inflamed appendix is lying, on active movement. This in turn often leads the child to avoid strenuous games and so to keep away from other children and cling to its mother's apron strings. Subconsciously it feels that it is not quite as other children are and all sorts of behaviour disturbances may arise. It is often good-looking and usually nervy and excitable, for the mildly inflamed appendix seems to act as a nervous irritant. On examination the most constant and characteristic feature is the presence of Ligat's reflex over the appendicular spot, but examination for this must be very gentle or the child's confidence will be lost and any replies untrustworthy. Often it is best to ask no questions at all, for if the hyperaesthesia is at all marked the little patient's whole frame will be felt to stiffen as the spot is gently pinched, or next time it is examined it may cry instead. Usually there is tenderness on deep but gentle palpation, and some degree of muscle rigidity or guarding can be appreciated. The reality of this rigidity can be demonstrated by looking at the child with its shoulders bare, for the right shoulder will often be found an inch or so lower than the left owing to the constant excessive tone of the right abdominal muscles. (There are of course other causes of this crooked stance, but in my experience a chronic mild appendicitis is the commonest, and it is not normally present in a true acute appendicular flare-up, for relatively few of these cases ever progress to the common acute appendix.)

More might usefully be said about this condition, but I will only add that in these cases one can often wait months or years before deciding whether or when operation is desirable. It is, I think, commoner in girls than in boys, and, while the latter show some tendency to overgrow the condition, girls, I think, never do. If an operation is performed it must be done in such a way as not to terrify the child, and then the results for child, parents, and doctor are almost invariably gratifying.

The other point I would raise is that I am disappointed Professor Capon said so little about medical treatment. I know that it is fashionable to decry medicines, and especially glycerophosphates, but the fact remains that over 30 years I have found one preparation which does stimulate the appetite of these children in a remarkable way. I have seen it do it many times with my own children, and hundreds of mothers in Winsford have seen it with theirs. It is a long, complicated prescription known as Dr. Robin's formula for syrup. glycerophos. co. As it seems to vary according to the maker, I should say that for 25 years I have used that supplied by James Woolley & Co., of Manchester. I know of nothing else to touch it for stimulating appetite, though there may be others. I fancy that the most active principle may be the kola, but, as Lord Horder wrote of a much simpler mixture[2]: "How much of the good which this preparation has done to humanity since some genius first invented it is due to any one of its ingredients none can say . . . nor at which part of the gastro-intestinal tract."

Of course there is a lot to be said against treating a symptom such as loss of appetite, but experience proves that if a child begins to eat well it usually begins to improve, and, though many of the conditions mentioned by Professor Capon may be pending or actually present, a healthy appetite goes a long way to make a healthy child, and these underlying or accompanying disorders tend to disappear.—I am, etc.,

Winsford, Cheshire. W. N. LEAK.

REFERENCES

[1] *British Medical Journal*, 1935, 2, 84.
[2] *Practitioner*, 1953, 170, 8.

Eczema and Reticulosis

SIR,—The description of a case of Sézary's reticulosis with exfoliative dermatitis by Drs. Harold T. H. Wilson and J. Fielding (*Journal*, May 16, p. 1087) has drawn attention to an important association which is more common than published evidence would indicate. It is customary to regard the reticuloses as a single pathological process which can adopt a number of histological and clinical appearances, either pure or mixed.[1] The frequency of the eczema–reticulosis association is evident from my series of approximately 60 malignant reticuloses, of whom eight patients have suffered from eczema (four with Hodgkin's disease and four with lymphosarcoma). All eight patients are living, with a relatively benign form of reticulosis. In seven patients the eczema developed either at the time of the appearance of the reticulosis or within the preceding year, while in one patient eczema antedated her lymphosarcoma by 10 years. Six patients have had a recurrence of eczema following the diagnosis of reticulosis. With one exception, the eczema was localized and controllable by superficial *x*-ray therapy

or skin lotions. Mycosis fungoides has been excluded in every instance. As a reticulosis usually has a subclinical onset several months before palpable lymphadenopathy, it may be assumed that the two pathological processes have had a concurrent onset in seven patients. Further evidence of the association of allergy with reticulosis is afforded by one patient aged 48 years who developed lymphosarcoma in 1947 and in each succeeding summer has had severe hay-fever. She had been well before 1947. This does not apply to the three cases of asthma in my series, one of whom lost his asthma five months before the onset of the reticulosis, while in two an existing asthma became less severe with the onset of reticulosis. These 12 cases would appear to offer evidence of a powerful antigenic factor in the early stages of the malignancy. An initial attack of eczema, hay-fever, or asthma may precede the appearance of a carcinoma.[2]

May I conclude with a plea to radiotherapists to investigate the incidence of allergic disorders in their patients with malignant lymphomas as a possible key to the riddle of cancer ?—I am, etc.,

Wellington, New Zealand. J. LOGAN.

REFERENCES

1 Custer, R. P., and Bernhard, W. G. (1948). *Amer. J. med. Sci.*, **216**, 625.
2 Logan, J., and Saker, —. (1953). *N.Z. med. J.*, **52**, 210.

Genetics and Clinical Research

SIR,—It was interesting to see your leading article on this subject (*Journal*, August 8, p. 326). I was sorry, however, to miss in it the name of one of the pioneers in this field, Professor Julius Bauer. This omission appears the more regrettable as he is well known to you, and you devoted a first leading article to his work in the past (*Journal*, April 24, 1943, p. 510).

Several of the problems mentioned in your present article have been studied intensively by J. Bauer and reported in original papers. I would like to mention—among many others—his studies on genetic factors in cancer and ulceration of the stomach ; but, of course, in 1943 you yourself referred to the importance of his book *Constitution and Disease*.[1]—I am, etc.,

London, S.W.3. V. C. MEDVEI.

REFERENCE

1 *Constitution and Disease : Applied Constitutional Pathology*, 1942, Grune and Stratton, New York.

Dr. Samuel Gee

SIR,—May I point out that, being misled by Sir Philip Manson-Bahr (*Journal*, August 1, p. 284), you have given Dr. Samuel Gee a title in your leading article (p. 266) ? The story which was current in St. Bartholomew's Hospital 50 years ago was that one of his colleagues saw Dr. Samuel Gee in the Square, wearing a fine fur coat, and expressed the hope that he might receive some recognition for looking after a royal personage. Gee replied: "They asked me if I would like to be made a baronet, but I said I would much rather have a fur coat, and this," fingering the lapel, "is it." —I am, etc.,

London, W.1. GEORGE GRAHAM.

Upside Down

SIR,—Dr. Wilfred Harris (*Journal*, August 8, p. 297) provokes us by saying : "We know from the optics of the eye that the image of any object seen is inverted on the retina. Why then do we see objects in their correct position and not upside down ?" To see everything, including ourselves, as "upside down" would merely mean "upside down" in relation to perceptions derived from the other sense organs, and the position in space of the representation on the retina or visual cortex will have nothing to do with this relationship.

The young children he reports as seeing "all test letters upside down" are perhaps more mysterious than he makes out. If they simply saw everything upside down then they would be expected to draw the right way up, so that when they looked at their drawing and saw it inverted it would match the object they were attempting to portray. Perhaps they are drawing from memory.—I am, etc.,

H. ASHER.

Physiology Dept., Birmingham University.

Myocardial Infarction

SIR,—The article by Dr. H. E. S. Pearson (*Journal*, July 4, p. 4) once again demonstrates the reduction in mortality and complications achieved by the use of anticoagulant therapy. Cardiac failure and its effects are important early complications which might be included when considering this subject. I have recently had under my care a man doing well under anticoagulant therapy with complicating congestive failure. Although the latter was treated, at the end of the third week he developed a sudden passive pleural effusion which proved fatal before medical aid could reach him.

Dr. R. A. Murray Scott (*Journal*, July 18, p. 151) quotes three references in support of his claim that prothrombin depression need not be taken below 60% of normal. I think these deserve some comment. Wright *et al.* achieved a 6% incidence of thrombo-embolism, with prothrombin levels of 20% and less. However, they went on to analyse their failures, and found that out of 38 such cases only four were actually in their desired therapeutic range of prothrombin depression, the others having escaped from control. Furthermore, they concluded that a considerable proportion of these failures were in fact due to inadequate prolongation of the prothrombin time. Burt *et al.*[2] described a series of cases of thrombo-embolism occurring in peripheral blood vessels, and did not describe any cases of coronary thrombosis. Their results are not therefore really comparable to the subject under discussion. Peters *et al.*[3] record the surprisingly optimistic figure of only 2% of thrombo-embolic complications in their series of 50 cases, rather than the 6% credited to them by Dr. Murray Scott. Their mortality rate of only 4% is also well below that of other writers, who usually put it at about 13.8%.[4] However, their patients were selected ones in whom they claimed to have demonstrated an increased coagulability of the blood. They do not give details of the proportion of severe cases, or many clinical details. In view of these circumstances I feel that their results should be interpreted with reserve.

Finally, I would like to quote Gilchrist's opinion[5] that adequate anticoagulant therapy has a favourable influence on shock in support of my plea for the prompt use of this treatment by the general practitioner.—I am, etc.,

Twickenham. DAVID WHEATLEY.

REFERENCES

1 *Amer. Heart J.*, 1948, **36**, 801.
2 *British Medical Journal*, 1949, **2**, 1250.
3 *J. Amer. med. Ass.*, 1946, **130**, 398.
4 Tulloch, J. A., and Gilchrist, A. R. (1950). *British Medical Journal*, **2**, 965.
5 Ibid., 1952, **2**, 351.

The Egg Maligned

SIR,—My morning bacon and egg is being impugned by Dr. H. W. Fullerton *et al.* (*Journal*, August 1, p. 250). It is literally blood-curdling, and, despite the cautious wording of the authors, already many a casual reader of the daily press may be switching to a Continental breakfast. It is hard to relate our restricted consumption of fats during the last years to the rising incidence of coronary thrombosis. For my own part I shall continue to take an English breakfast, and shall comfort myself with the reflection that coagulation has its virtues and that not every clot is clumsy.

As a surgeon I see arteriosclerosis and secondary thrombosis mainly in the lower limbs of patients complaining of intermittent claudication. In the last few years I have advised over 300 such patients, and, though I know nothing of their breakfast habits, I cannot recall a single one who was not an inveterate cigarette smoker. The link between cigarettes and arteriosclerosis in the lower limbs appears to me to be almost invariable and quite inescapable. I can recall only one patient who was able to give up smoking for even a few weeks, and he, poor fellow, died of coronary

thrombosis shortly after an operation. About coronary thrombosis itself I must write with more caution, because this is a disease which, in general, I have not studied. In claudication, however, the coronary accident is so common, and so frequent a cause of death, that the two do appear to be related—at least to each other if not to tobacco.

Your authors say that "the pathogenesis of arteriosclerosis remains obscure." Without any reference to tobacco, they indict, albeit tentatively, the egg. This seems so unfair that it has stung me into writing this letter and saying something I have been wanting to say for a long time.—I am, etc.,

Liverpool, 7. CHARLES WELLS.

The Role of the Pathologist

SIR,—Drs. M. Goldman and D. H. Miller (*Journal*, July 25, p. 227) accuse pathologists of being "self-appointed judge and juries of their clinical colleagues." May I remind them that they appear in court as witnesses on oath and answer the interrogation of judge, counsel, or coroner to the best of their ability? They are not permitted to give a spontaneous expression of their views. They are in fact already "confined to a statement of facts and, at the most, an expression of opinion as to the cause of death."—I am, etc.,

Keighley. IAN STEWART.

Malaria in Ex-Servicemen

SIR,—I was very interested to read the letter by Drs. A. F. Knyvett and F. D. Schofield (*Journal*, August 8, p. 339) on malaria in ex-Servicemen. I thought the following two cases might be of interest.

Case 1.—A Territorial soldier, aged 22, admitted with pyrexia and generalized muscular aches of 24 hours' duration. No diagnosis was made at this time because of the bizarre and seemingly unrelated nature of the symptoms, which included vague abdominal pains and headaches. A peripheral blood smear taken during a rigor 96 hours after admission revealed the schizonts of *Plasmodium vivax*.

Case 2.—A regular soldier, aged 24, also admitted with a very similar history of malaise and pyrexia, but he had carried on for six days without reporting sick. This case also had many of the features of an "influenzal" illness, but here again a peripheral blood smear examined at 24 hours demonstrated the schizonts of *Plasmodium vivax*.

Both these patients were seen within six weeks of each other and had served in Korea last summer. One had returned eight months ago and the other six months ago. No previous history of malaria was obtained, although the first patient had had a mild pyrexial illness with one rigor shortly after returning to this country. Both men had taken the issue of proguanil whilst overseas.

First impressions in both—namely, that they were cases of influenza—tended to obscure the diagnosis, which in the first was not made until the periodicity of the rigors was recognized after 96 hours. There were no other signs in either case, such as splenomegaly, to assist in arriving at the diagnosis.—I am, etc.,

Holt, Norfolk. W. A. CRABBE.

Polyarthritis in Rubella

SIR,—I was most interested to see that Dr. K. H. Pickworth (*Journal*, August 8, p. 339) and Dr. G. W. Lewis (*Journal*, July 18, p. 149) found, as I did (*Journal*, June 20, p. 1388), that the complication of polyarthritis in rubella seemed to be confined to adult women. I can think of no other infectious illness affecting both children and adults which behaves so differently in the group of adult women only, and in this curious fact there may be hidden some clue to the aetiology of the arthritis. Dr. Pickworth suggests that the polyarthritis of rubella is allied to the aches and pains that occur at the beginning of the majority of infections, and he goes further and suggests that all these phenomena are allergic and allied to serum sickness.

I cannot agree, for the following reasons: (1) The polyarthritis continued in my experience long after any slight fever associated with the rash, and in 5 out of my 16 cases first appeared on or after the second day of the illness. (2) The severity of the pains in the joints was out of all proportion to the mildness of the illness itself. (3) If the polyarthritis were in the nature of an allergic response it would be reasonable to suppose that there might be an accompanying eosinophilia and that the joint symptoms would subside if antihistamine drugs were given.

In two of my cases blood films were examined for eosinophilia and there was none. Four of my cases received diphenhydramine, 50 mg. three times a day, without any alteration of joint symptoms.

Four cases is, admittedly, a small number, but soon after plans were laid for investigating the possibility of the allergic nature of the arthritis the epidemic died out.—I am, etc.,

Wantage. I. S. L. LOUDON.

Intravenous Picrotoxin for Barbiturate Poisoning

SIR,—Intravenous picrotoxin, as advocated by Dr. R. S. Saxton (*Journal*, July 25, p. 227), is not without hazard. I have seen a patient on more than one occasion in coma from barbiturate poisoning having convulsions as a result of picrotoxin therapy, while in no way coming out of the coma. In serious cases, which nowadays occur not infrequently in the course of a routine "take in," gastric lavage is always indicated, and hospital treatment should not be denied to these patients. One sees cases surviving after three or more days in coma, and psychiatric aftercare may be instituted speedily under in-patient conditions.

All cases recently reviewed in a Scandinavian paper[1] were treated with amphetamine, as picrotoxin was considered too toxic for routine use.—I am, etc.,

Collingbourne Ducis, Wilts. B. H. BASS.

REFERENCE

[1] Nilsson, E. (1951). *Acta med. scand.*, suppl. 253.

Please Wash Your Hands

SIR,—All G.P.s, not to mention the general public, must by now be heartily tired of the gastro-enteritis which has become endemic in this country in the last few years. Public health activities seem confined to looking for carriers after major outbreaks, but the number of carriers must be legion and this seems a hopeless task. There seems to be some agreement that nine-tenths of the trouble would stop if the public were educated to wash their hands after visiting the lavatory, but no one educates them.

I should like to suggest a simple solution. If every public lavatory abolished the charge for a wash, and exhibited a notice saying, "Please wash your hands before leaving. No charge," the result would probably be as effective as in the two precedents of "Please do not spit" and "Please adjust your dress before leaving." Once it became a habit in public lavatories it would soon become a habit elsewhere.

If the Ministry of Health offered to pay local authorities the cost, it would soon make a profit from the reduced number of prescriptions for sulphonamides and antibiotics. Is it possible for our public health colleagues to use their influence in bringing about this reform?—I am, etc.,

Ashtead, Surrey. W. EDWARDS.

Brain of Kernicteric Infants: An Appeal

SIR,—I would be very grateful for specimens of the brain of kernicteric infants. I am investigating the pigments occurring in the blood and tissues of infants affected with haemolytic disease of the newborn, and there is at present an extreme shortage of post-mortem material from infants dying of kernicterus. The specimens should preferably be unfixed, as formalin and alcohol seem to affect the pigments.

If any specimens occur I can arrange for them to be collected within a radius of 100 miles of Manchester if a telegram or 'phone call is made to URMston 4022 or SALe 3111.—I am, etc.,

Park Hospital, Davyhulme, Urmston, nr. Manchester. D. C. A. BEVIS.

Obituary

Dr. S. M. VASSALLO, formerly a senior specialist officer in surgery in the Colonial Medical Service, died suddenly at his home at Epsom, Surrey, on July 23, at the age of 62. Salvatore Michael Vassallo was born in Malta on January 28, 1891, and received his medical training at the University of Malta, where he graduated M.D. in 1913, gaining a Government exhibition for first place. He then came to England as a postgraduate student, and in 1914 entered the Colonial Medical Service, being posted to the Leeward Islands as a medical officer. From 1917 to 1919 he served as a captain in the R.A.M.C., and was mentioned in dispatches. On demobilization he resumed his work in the Colonial Medical Service, this time in Uganda, returning to England to take the D.T.M.&H. in 1922. In 1925 he was appointed resident surgical officer in Zanzibar, the title of his post being changed to that of senior specialist officer ten years later. In 1928 he was admitted F.R.C.S.Ed. While in Zanzibar Dr. Vassallo was medical adviser to the Sultan from 1925 to 1939, and he was President of the Zanzibar Branch of the British Medical Association in 1929–30, and again in 1934–5. In 1936 the insignia of the third class of the Order of the Brilliant Star of Zanzibar was conferred upon him; he also received the King's Silver Jubilee Medal in 1935 and the Coronation Medal in 1937. When war broke out again in 1939 Dr. Vassallo immediately re-entered the R.A.M.C. as a lieutenant, being promoted to major in three months, and served first as a surgical specialist and then, from 1942, as the officer in charge of a surgical division. He remained in the Army until November, 1948, by which time he had attained the rank of lieutenant-colonel. He was mentioned in dispatches in 1941. On his return to civilian life he became senior surgical specialist at the Royal Herbert Hospital, Woolwich, a position he held until his retirement last year. Dr. Vassallo leaves a widow and one daughter.

Dr. B. Spearman, late Director of Medical Services, Zanzibar, sends the following appreciation: For 10 years I was in constant touch with Dr. Vassallo and saw that with diverse nationalities—European, Arab, Indian, and African—he proved a boon and a blessing. A surgeon of outstanding abilities, he never spared himself and worked long hours in the tropical heat, and one sometimes wondered at his staying capacity. While on leave he continued his studies and took the Edinburgh F.R.C.S. He was also a capable and wise physician and thoroughly experienced in tropical diseases. Everyone, whatever his faith or creed, put his faith in Michael, and his patients came from India and all parts of East Africa. He retired in 1939, only to rejoin the R.A.M.C. In his spare time he served as honorary secretary to the East African Pensioners' Association, and all those who received benefits through this organization owe him a big debt of gratitude. Knowing seven languages, he did much abstracting work for *Abstracts of World Medicine* and *World Surgery*, and for the *Journal of Urology*. The sympathy of all who knew him, of whatever creed or colour, whether in the United Kingdom or scattered throughout the British Empire, goes out to his wife and daughter in their irreparable loss.

Lieutenant-Colonel A. B. Dempsey, R.A.M.C., writes: Michael Vassallo, after a distinguished surgical career in Zanzibar for 25 years, brought to the Army Medical Services a wealth of clinical wisdom and practical surgical experience when he left a well-earned retirement to volunteer at the outbreak of the last war. He served with distinction in the Middle East for some years, but it is for his work at the Royal Herbert Hospital, Woolwich, from 1944 to 1952 that he will best be remembered. During this period many regular surgeons passed through his hands when he was in charge of the surgical division. They were working, in every case successfully, for higher surgical qualifications, and their successes were in no small part due to his kindly advice, teaching, and encouragement, and to the fact that at considerable personal inconvenience he carried a very heavy load himself in order to allow them more time for study. "Vass," as he was known to his many friends in the Royal Army Medical Corps, will be greatly missed. His quiet smile, often hiding an almost impish sense of humour, endeared him to all his juniors. He will be remembered with affection and gratitude by surgeons now serving in many parts of the world, who owe him much.

By the sudden death of Dr. SAMUEL ROSE at his home on July 1 at the age of 55, Wimbledon has lost a popular and skilful general practitioner. Samuel Rose was born in New York on October 5, 1897, and was educated at University College School, London, and at Guy's Hospital, where he qualified in 1919. Two years later he took the London degrees of M.B., B.S. After a house-surgeoncy at Guy's he became senior assistant medical officer at Fulham Infirmary. In 1924 Dr. Rose settled at Wimbledon, in partnership with three other doctors, and soon developed a large practice. His professional skill, his kindly manner, and his sympathetic approach to other people's problems made him a popular member of the local community. For many years he was a member of the honorary staff of Wimbledon Hospital, and he acted also as deputy police surgeon and Treasury medical officer for West Wimbledon. In the last war he served as a medical officer in the Home Guard, a heart affection preventing him from giving full-time service in the Forces. Despite this disability, which ultimately caused his death, he continued his work throughout the war, and many local residents, including those injured in air raids, owe much to his ability as a surgeon. Dr. Rose had wide interests, and his genial manner and great vitality brought him many friends. Interested in all kinds of sport, he was an enthusiastic member of the Royal Wimbledon Golf Club. He leaves a widow and two daughters.

Dr. J. R. HALL died at Wingate, Co. Durham, on July 10 at the age of 70. Born on December 6, 1882, the son of the late Mr. W. T. Hall, J.P.—the first chairman of the Bellingham Rural District Council—John Robertson Hall was educated at Dollar and Edinburgh Academies and at Edinburgh University, where he graduated M.B., Ch.B. in 1907. Soon after graduation he joined his brother, the late Dr. W. T. Hall, in practice at Newcastle-upon-Tyne. In 1911 he set up his plate on his own account at Fence Houses, Co. Durham, and there he remained until 1938, when he moved to Wingate, except for a period of service in the R.A.M.C. in the war of 1914–18. He was invalided out of the Army after receiving wounds in the Battle of the Somme. Always attracted to the work of the St. John Ambulance Association, to which he had been an examiner since 1914, Dr. Hall was a popular lecturer to first-aid classes. He was appointed a Serving Brother of the Order of St. John of Jerusalem in 1937. The outbreak of the last war in 1939 saw an increase in his activities on behalf of the Association, but he found time to lecture also on air-raid precautions and to serve on medical boards. In addition he was a captain in the Home Guard. Outside his profession Dr. Hall derived much satisfaction from the study of Border history, and, having a good memory, he could be relied upon to provide many an interesting reminiscence. He leaves a widow.

The untimely death of Dr. LOUIS SHELDON at the early age of 49 has deprived the practice of medicine in Willesden and Wembley of one of its outstanding figures; for Louis Sheldon was one of that breed of men who shed lustre on their profession, and to whom hard work did not spell hardship. Born in South Africa on October 30, 1903, Sheldon came to England at the age of 21, and qualified L.M.S.S.A. from the London Hospital in 1926. He took over an old-established practice in Willesden soon afterwards, and there

for 25 fruitful years he was guide, philosopher, and friend to an ever-increasing circle of patients. He allied clinical acumen of a high order with boundless energy, and inevitably acquired a splendid reputation as a practitioner in the best family-doctor tradition. He did not spare himself, and on many an occasion Sheldon would excuse himself to his guests—there was nothing he liked better than to play the host—to go and visit a patient in response to an urgent message. This spirit was apparent even during his last illness, when he was to be seen, driven by his son, for he was no longer able to drive his car himself, doing his round of visits, an ill man and obviously suffering. During his busy life he found time for broader interests and served on the executive committee of the Willesden Division of the British Medical Association, where his unobtrusive good sense made him a valued member. He was well known at the Willesden General Hospital, where he worked for some time as clinical assistant, and at the West End Hospital for Nervous Diseases. His local interests were many. He served as medical officer to the local Red Cross detachment, St. John Ambulance Brigade, and the Willesden Air Training Cadets, and, in another field, as medical officer to the Hendon Football Club, a reflection of his youthful enthusiasm for soccer and his days in the London Hospital first eleven. During the last war he was one of those whose work at the Stonebridge first-aid post during the worst days is still remembered. All in all he left his mark on Willesden, and his death leaves a gap which will not easily be filled. His patients' sorrow can best be epitomized in the inscription on a wreath sent by one of them—"To our dear doctor and friend." His colleagues in Willesden will not soon forget him. To his widow, who bore the great strain of his last illness with wonderful courage, and to his son, who carries on the medical tradition of his father, his colleagues and friends offer their heartfelt sympathy.—M. M.

Medico-Legal

FATAL PENICILLIN INJECTION

At an inquest held in Kingston-upon-Hull on July 14 the coroner recorded a verdict of misadventure on a woman aged 41 who had died from anaphylaxis following an injection of penicillin administered for pyrexia during delivery.

After a normal pregnancy the patient was admitted to hospital at 10.30 a.m. on June 30. The same evening she was still in early labour and was given morphine ¼ gr. (16 mg.). On the evening of July 1 she developed a temperature of 101° F. (38.3° C.). No cause for the pyrexia was apparent, but she was given 400,000 units of procaine penicillin intramuscularly at 6.30 p.m. At 7.30 p.m. the patient vomited; two minutes later she had a labour pain, and while at the height of this pain she suddenly collapsed. She immediately became unconscious, and her breathing was stertorous as in cerebral haemorrhage. Despite all attempts at resuscitation she died within a few minutes. The patient had had previous injections of penicillin, though she had no history of previous reactions to it. Other patients had received injections from the same batch of penicillin without ill effect.

Dr. James Ross McKenzie, senior registrar, Kingston General Hospital, Hull, who did the post-mortem examination, said there were signs of asphyxia, with many petechial haemorrhages over the surfaces of the lungs. He gave the cause of death as anaphylaxis following the injection of penicillin. He was able to find only two such cases reported in this country out of the millions of penicillin injections which had been given. Only one such case had been reported in the American literature.

The coroner, in summing up, suggested that it would be a wise precaution for any patient who had had a previous reaction from penicillin to tell a new doctor about it before penicillin was administered.

Universities and Colleges

UNIVERSITY OF OXFORD

The following medical degrees were conferred on June 25:

D.M.—W. D. M. Paton, R. Seidelin, G. Loewi.

B.M.—R. B. Roe.

On July 1, in connexion with the centenary of Cecil Rhodes and the jubilee of the Rhodes scholarships, the honorary degree of D.C.L. was conferred on W. G. Penfield, O.M., Honorary Fellow of Merton College, Director of the Montreal Neurological Institute, and Professor of Neurosurgery in the University of McGill.

In Congregation on July 18 the following medical degrees were conferred:

D.M.—R. M. Mason, J. T. Wright.

B.M.—B. C. Davies, B. J. Drake, W. A. F. Macdonald, H. Merskey, P. S. Mitchell, G. L. Feinstein, G. C. Fisk, M. R. C. Heffernan, M. P. Carter, J. G. Ross, J. H. Fairley, P. D. P. McGrath, C. J. Good, I. E. Hughes, V. Parsons, R. W. G. P. Best, J. B. L. Gee, J. A. Kay, G. A. Rose, Christian A. K. Carritt, Diana J. Collins, Rosalind M. Rewcastle, *C. E. Elliott, *N. R. Garden, *R. E. Gillson, *F. I. Caird, *J. I. McFeeters, *Priscilla A. Clark-Maxwell.

The Theodore Williams Scholarship in Human Anatomy for 1953 has been awarded to Oliver Wolf Sacks, Scholar of Queen's College.

The Radcliffe Scholarship in Pharmacology has been awarded to Antony Babington Herring (Brasenose College) and John Verrier Jones (University College).

Dr. R. S. Creed has been elected a member of the Board of Studies for Psychology for two years from October 1, 1953.

*In absence.

UNIVERSITY OF GLASGOW

The following medical degrees were conferred on July 4:

M.D.—[1]P. A. Duke, [2]G. M. Edington, [2]C. R. Forrest, [4]I. MacGillivray, [3]A. F. McLean, W. W. W. McNeish, D. G. Scott.

M.B., Ch.B.—J. Allan, J. M. Atkinson, J. T. B. Bain, Muriel M. E. Barr, [4]J. S. Beck, Sheila J. D. Black, M. Blair, D. A. P. Brown, D. D. Bryson, T. H. L. Bryson, R. T. Cameron, J. S. Cant, R. L. K. Colville, I. J. Coulthart, J. L. C. Dall, A. Davidson, J. S. H. Davidson, J. A. S. Dickson, H. P. Dinwoodie, A. Donnelly, J. A. Duncan, I. E. Farrington, H. C. Ferguson, A. H. Findlay, Margaret E. Finlayson, T. Forrest, J. Frame, W. Gallacher, H. H. Gebbie, Lilian M. Gibson, Biruta R. Giedraitis, I. E. Gillespie, S. S. Graham, J. H. Graham-Marr, M. Haase, W. A. McL. Hall, L. Harris, D. D. Hart, Grace J. K. Harvey, J. C. Henderson, Martha C. Howat, R. McN. Howie, R. M. Humble, R. Hume, Isobel H. Hunter, A. G. Hutchison, Margaret W. Irwin, G. H. Johnson, J. A. Johnston, Margaret N. S. Johnston, C. C. Keay, J. D. Kinloch, J. W. S. Knox, K. A. Kwarko, T. J. Lees, H. C. Leslie, J. G. Lindsay, L. E. Lonergan, E. C. McCracken, Morag C. McCulloch, J. C. H. McDonald, C. G. McEwen, A. McGowan, Berthea J. MacGregor, W. L. MacIndoe, Eleanor M. MacIver, T. M. McKendrick, Catriona Mackenzie, A. C. Maclachlan, K. M. McLaren, J. C. Maclaurin, Lindsay McLeman, P. B. McMain, J. P. McMillan, G. W. Macnab, Christine McNair, [4]M. W. McNicol, W. A. Maley, T. S. Mann, F. Mariotti, J. J. F. Merry, H. McI. Morgan, Elizabeth A. Mowat, I. S. Murray, J. W. Myles, G. F. Nabi, E. G. Oram, J. R. Paterson, P. M. Peacock, J. G. Provan, Maria A. Ratzer, C. B. Rennick, C. J. C. Renton, J. A. Riddell, A. Robertson, K. M. Robertson, A. J. Rosin, Margaret C. Russell, R. C. I. Russell, R. J. Scott, R. Shields, A. M. Short, [4]J. D. Sleigh, C. C. S. Slorach, Margaret B. Smith, M. G. H. Smith, N. M. Smith, V. B. Smith, Kathleen A. R. Smith, W. T. Sommerville, C. Sorbie, Isobel Speirs, J. M. Stark, Norah E. Stewart, J. R. Styles, V. Sweeney, Lilian M. G. Tait, T. E. Torbet, J. J. Treanor, R. D. Unkles, D. H. Urquhart, J. M. T. Warnock, J. McI. Williamson, A. Wilson, D. W. Wylie.

[1]*In absentia.* [2]With high commendation. [3]With commendation. [4]With honours.

UNIVERSITY OF LONDON

Dr. J. D. N. Nabarro and Dr. Howard Nicholson have been recognized as teachers of medicine in the University at University College Hospital Medical School.

The Sir William Dunn Scholarship for 1953–4 has been awarded to Barbara Joan Boucher (London Hospital Medical College).

The title of Professor of Experimental Pathology in the University has been conferred on Dr. A. A. Miles in respect of the post held by him at the Lister Institute of Preventive Medicine.

Dr. George Dennett Lumb has been appointed to the University Readership in Pathology tenable at Westminster Medical School, from October 1, 1953.

Dr. W. St. C. Symmers, senior lecturer in the University of Birmingham, has been appointed to the University Chair of Morbid Anatomy tenable at Charing Cross Hospital Medical School.

Dr. J. H. F. Brotherston, Senior Lecturer in Public Health at the London School of Hygiene and Tropical Medicine, has been appointed to the University Readership in Public Health tenable at that school.

The Mary Scharlieb Research Studentship has been awarded to Dr. Andrew William Anderson for the session 1953–4 in the first instance.

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN BACTERIOLOGY.—A. M. Cook, N. G. Fowler, K. A. Lim, D. McKenzie, Janet J. Mackintosh, D. J. H. Payne, L. Robertson, D. N. Sengupta, P. H. A. Sneath (awarded a mark of distinction), K. R. Wallace, J. E. M. Whitehead.

ACADEMIC POSTGRADUATE DIPLOMA IN PUBLIC HEALTH.—I. Ash, D. E. Boye-Johnson, R. Bradley, J. H. Brodie, J. Carlton, Gwen S. Clark, C. Eid, A. J. Essex-Cater, R. S. Gibson, G. J. Glynn, L. P. Harington, I. K. Hay, Winifred M. Hiscock, G. B. Hopkins, I. A. Hussein, Dorothy D. Jones, F. R. S. Kellett, A. J. I. Kelynack, J. H. Lewis, *Khoon-Huat Lim, B. Mahadevan, G. P. Merson, H. Mowschenson, F. G. Neild, B. Nicholson, *W. F. Ross, S. Sandmo, M. C. Sanyal, W. Sheffield, J. H. Taylor, A. M. Thomson, D. E. Thompson, G. F. Willson, A. B. Wittek, C. H. Wood, D. Yarom, A. Zahra, A. A. Zaki.

ACADEMIC POSTGRADUATE DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—E. B. Bright, P. Jordan.

The following candidates have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN MEDICAL RADIOLOGY (DIAGNOSIS).—N. L. Bucky, M. A. Harris, K. N. Kamdar, J. K. Lundie, G. A. Medhurst, D. MacK. K. Muir, J. V. Tillett, L. E. Wolpert, M. Ziman.

*Awarded a Mark of Distinction.

UNIVERSITY OF LEEDS

Dr. Geoffrey Watkinson, lecturer in the Department of Medicine, has been granted leave of absence for the session 1953–4 to enable him to take up a Rockefeller Travelling Fellowship.

The Services

Major-General F. Kingsley Norris, C.B.E., D.S.O., E.D., R.A.A.M.C., has been appointed Honorary Physician to the Queen, and Colonel K. B. Fraser, E.D., R.A.A.M.C., Honorary Surgeon to the Queen.

Major-General F. C. Hilton-Sergeant, Q.H.P., late R.A.M.C., has been appointed Commandant and Director of Studies, Royal Army Medical College, in succession to Major-General F. R. H. Mollan, C.B., O.B.E., M.C., Q.H.S., late R.A.M.C., who is retiring.

Colonel A. Swindale, C.B.E., T.D., has been appointed Honorary Colonel of a T.A. Unit in succession to Colonel A. H. Whyte, D.S.O., T.D., whose tenure has expired.

A *Supplement* to the *London Gazette* has announced the following appointments in recognition of gallant and distinguished services in Korea:

C.B.E. (Military Division).—Colonel G. L. M. Smith, O.B.E., C.D., R.C.A.M.C.

M.B.E. (Military Division).—Lieutenant-Colonel (Acting) R. A. Smillie, R.C.A.M.C.

A *Supplement* to the *London Gazette* has announced the following awards:

First Clasp to the Territorial Efficiency Decoration.—Major R. Barraclough, M B.E., T.D., and Captain (Honorary Major) H. R. Vernon, R.A.M.C.

Territorial Efficiency Decoration.—Major (Honorary Lieutenant-Colonel) J. B. McEwen, M.C., and Captain (Honorary Major) H. R. Vernon, R.A.M.C.

Vital Statistics

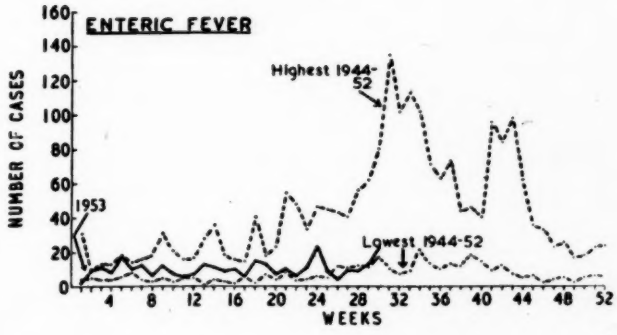
Poliomyelitis

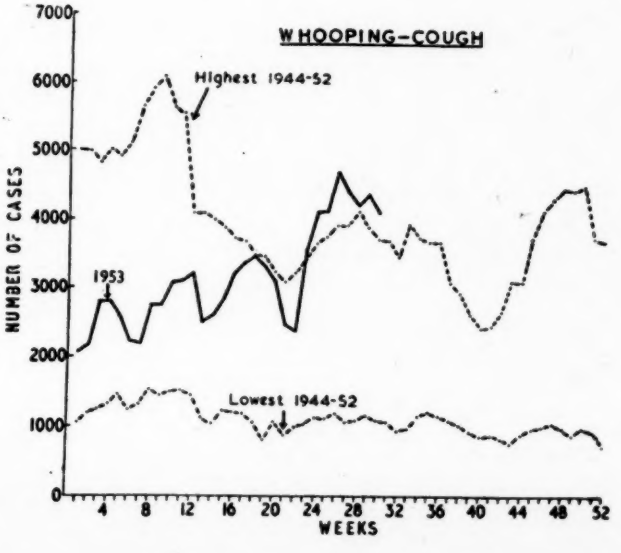
Poliomyelitis notifications (uncorrected) in the week ending August 8 (31st week of the year) were as follows: paralytic, 181 (167); non-paralytic, 116 (103); total, 297 (270). This is an increase of 27 compared with the previous week, the figures for which are in parentheses. The individual districts which have notified 20 or more cases in the year to August 8, with incidences per 100,000 in parentheses, are as follows: Southend-on-Sea C.B., 37 (24.42); Liverpool C.B., 25 (3.16); Birmingham C.B., 46 (4.11); Coventry C.B., 76 (29.12); Leicester C.B., 22 (7.69); Lewisham M.B., 22 (9.69); Blackpool C.B., 21 (14.26); Camberwell M.B., 20 (11.04); Islington M.B., 21 (8.92); Bournemouth C.B., 25 (18.00).

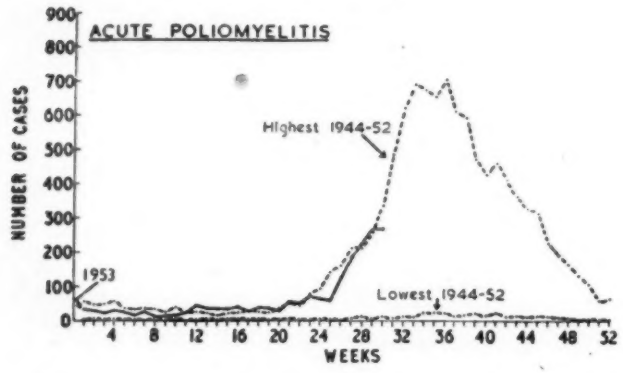
The seasonal rise in the notifications of poliomyelitis is not gaining momentum. The increase in paralytic cases was two less than in the previous week (14 compared with 16), and there is still hope that the curve will be like that for 1952. Although the seasonal rise is expected to continue, the outlook is somewhat more favourable than it appeared to be a month ago. Epidemic proportions are not being approached in any of the greater centres of population.

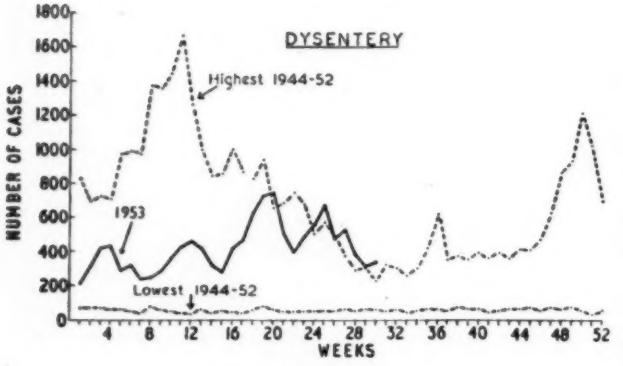
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Infectious diseases were less prevalent in England and Wales during the week ending August 1. The largest falls in the number of notifications were 807 for measles, from 4,394 to 3,587, 250 for whooping-cough, from 4,357 to 4,107, and 87 for scarlet fever, from 1,037 to 950.

The largest falls in the number of notifications of measles were 133 in Lancashire, from 804 to 671, and 71 in Somersetshire, from 162 to 91. A small decline in the incidence of scarlet fever was recorded in every region except the north-western, where the notifications were 42 more than in the previous week. The largest decline in the number of notifications of whooping-cough was 42 in London, from 389 to 347. 11 cases of diphtheria were notified, 6 fewer than in the previous week.

270 cases of acute poliomyelitis were notified during the week. These cases were 16 more for paralytic and 12 fewer for non-paralytic than in the preceding week. The chief centres of infection were still in the southern section of the country and were London 34 (Camberwell 5, Islington 5, St. Pancras 5, Lambeth 4), Essex 22 (Chelmsford M.B. 4), Middlesex 21 (Finchley M.B. 3, Heston and Isleworth M.B. 3), Southampton 19 (Bournemouth C.B. 8), Surrey 16 (Croydon C.B. 3, Reigate M.B. 3), Warwickshire 16 (Coventry C.B. 13), Kent 15 (Maidstone M.B. 4), Lancashire 14 (Liverpool C.B. 3), and Cheshire 10 (Nantwich R.D. 4).

334 cases of dysentery, 25 more than in the preceding week, were notified. The largest returns were Lancashire 67 (Blackburn C.B. 24, Manchester C.B. 15), London 35, Yorkshire West Riding 27, Durham 26, Middlesex 21, and Essex 18.

The largest outbreaks of food-poisoning notified during the week were 131 cases in Camberwell, London, 119 cases in Prestatyn, Flintshire, 100 cases in Wakefield C.B., Yorkshire West Riding, 69 cases in Consett U.D., Durham, and 54 cases in Lancaster M.B., Lancashire.

Week Ending August 8

The notifications of infectious diseases in England and Wales during the week included scarlet fever 690, whooping-cough 3,864, diphtheria 22, measles 2,730, dysentery 217, paratyphoid fever 12, typhoid fever 3, and food-poisoning 415.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 1** (No. 30) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	11	0	6	1	1	21	0	6	1	
Dysentery	334	35	84	1		135	19	45	0	
Encephalitis, acute	5	0	0	0		5	0	0	0	
Enteric fever:										
Typhoid	4	1	0	0	1	5	0	2	0	2
Paratyphoid	19	2	2	0	4	75	1	0	0	
Food-poisoning	769	169		0		231	17		0	
Infective enteritis or diarrhoea under 2 years				13	46				14	23
Measles*	3,587	80	83	83	82	7,363	844	96	128	193
Meningococcal infection	21	2	12	2		34	4	9	1	
Ophthalmia neonatorum	37	4	4	0		39	5	9	0	
Pneumonia†	222	11	99	0		247	10	142	4	1
Poliomyelitis, acute:										
Paralytic	167	22	13	18	10	157	23	9	6	1
Non-paralytic	103	12				96	10			
Puerperal fever§	232	18	5	0		260	31	14	2	1
Scarlet fever	950	55	97	20	31	1,173	113	144	16	53
Tuberculosis:										
Respiratory			129	32				121	32	
Non-respiratory			32	2				23	10	
Whooping-cough	4,107	347	369	55	37	2,040	97	91	70	133

DEATHS in Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	2	0	0	0	0	2	1		0	
Dysentery	0	0		0		0	0			
Encephalitis, acute		0			0		0			
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	5	1	1	1	2	7		2	0	
Influenza	3	1	0	0	0	6	0	2	0	
Measles		0	0	1	0		0		0	
Meningococcal infection		1	0				1	1		
Pneumonia	117	12	6	3	5	129	21		10	
Poliomyelitis, acute	10	0			0	6	3			
Scarlet fever		0	0	0	0		0		0	
Tuberculosis:										
Respiratory	85	13	10	1	3	83	8	16	3	
Non-respiratory		1	1	0	0		2	1	0	
Whooping-cough	5	1	0	0	1	0	0		0	
Deaths 0–1 year	201	30	24	9	13	204	23	15	10	
Deaths (excluding stillbirths)	4,284	590	455	87	130	4,177	609	523	96	
LIVE BIRTHS	7,974	1204	921	230	395	7,310	1090	898	244	
STILLBIRTHS	187	21	23			177	19	29		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Family Rehabilitation.—The Elizabeth Fry Memorial Trust has just issued an account of the establishment of the Spofforth Hall Recuperative Centre, to which mothers (and their children) are sent who fail to provide a satisfactory home for themselves and their families. The majority of the mothers have simply failed to cope with domestic problems and difficulties, and have reached a point when they have accepted defeat and allowed the home conditions to deteriorate. A small proportion of the families are those in which the parents have already been charged in the courts with neglecting their children. Instead of sending the mother to prison, often the prelude to the permanent collapse of the home, she can be put on probation and, with the consent of the Home Office, may be required to accept at least four months' residence at Spofforth Hall, which is near Harrogate. "In more human terms the results of homes which have failed are seen in the dispirited mothers and pathetic babies and children who come to Spofforth Hall." The home was established under the auspices of the Society of Friends, and the first families arrived last November. The demand for accommodation has grown rapidly since then, and the trustees have decided to adapt an extra wing of Spofforth Hall in order that three more families may be received. Although the cost of maintaining most of the families is met by statutory authorities, there is still need for generous public support of this worthy project.

Society of Apothecaries.—On August 18 the Society elected as Master Dr. H. Seaward Morley, as Senior Warden Sir Cecil Wakeley, P.R.C.S., and as Junior Warden Dr. N. S. Finzi.

NEW ISSUES

Journal of Neurology, Neurosurgery, and Psychiatry.—The next issue (Vol. 16, No. 3) will be available in a week's time.

Journal of Clinical Pathology.—The next issue (Vol. 6, No. 3) will be available in a week's time.

Issued quarterly; annual subscription £2 2s., single copy 12s. 6d. These journals are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Tuesday, August 25

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.—5 p.m., Professor John Fulton (U.S.A.), Harvey Cushing: A Biographical Appreciation.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Hales.—On July 1, 1953, at the London Hospital, London, E., to Mary (formerly Notley), wife of John Hales, M.B., B.S., a daughter—Kathryn Mary.

Scott.—On August 11, 1953, at the General Hospital, Neath, Glamorgan, to Dorothy, M.B., Ch.B. (formerly Wood), wife of Dr. B. K. Scott, a daughter.

Walsh.—On August 5, 1953, at Saint John, New Brunswick, Canada, to Ruth (formerly Broughton), wife of Peter Walsh, M.R.C.P., of 260, Germain Street, Saint John, New Brunswick, Canada, a son—Robert Edward.

DEATHS

Jhangiani.—On July 5, 1953, Parmanand Harumal Jhangiani, M.B., B.S., D.M.R.E., of Canonbury, London, N.

Legat.—On July 23, 1953, at his home, 8, Hughenden Road, Clifton, Bristol, Robert Eddowes Legat, M.B., C.M., aged 83.

McMichael.—On July 28, 1953, Arthur William McMichael, M.R.C.S., L.R.C.P., of 27, Frenchay Road, Weston-super-Mare, late of Vowchurch, Herefordshire, aged 85.

Rafferty.—On July 28, 1953, suddenly, at Clayton Hospital, Wakefield, Patrick Joseph Rafferty, L.R.C.P.&S.I. & L.M., of Westgate End House, Wakefield, Yorks, aged 54.

Raw.—On July 25, 1953, at Ardgay (Bonar Bridge), Ross-shire, Mary Raw, M.B., B.S., of Ravenswood, Low Fell, Gateshead, late of the Baptist Missionary Society's Dholpur Station, India.

Talbot.—On July 28, 1953, at his home, Coed-y-Castell, Deganwy, Caern., N. Wales, Philip Talbot, M.B., Ch.B., F.R.C.S., aged 72.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Sensitivity to Oil of Bergamot

Q.—*Is a skin reaction to oil of bergamot found only in certain sensitive individuals, or will it occur in anyone under appropriate conditions? What is meant by the term "photosensitivity," which is often used in describing bergamot reactions?*

A.—The skin reaction to oil of bergamot is found only in certain people. In these subjects the application of oil of bergamot to the skin results in a temporary increase in light sensitivity on that particular area of skin. The mechanism by which this occurs is not known, but the substances most often involved are of vegetable origin, and for this type of reaction the term "phyto-photo dermatitis" was coined by Klaber,[1] whose original work should be consulted.

REFERENCE

1 Klaber, R., and Wittkower, E. (1939). *Brit. J. Derm.*, **51**, 501.

Vaginitis in Girls

Q.—*What is the modern treatment of non-gonococcal vaginitis in small girls?*

A.—The organisms responsible for the vaginitis should first be determined by examination (direct smear and culture) of the discharge obtained from the vagina by a swab or fine pipette gently inserted through the hymeneal opening. The possibility of a foreign body in the vagina should be considered and excluded, especially if the discharge is blood-stained as well as purulent.

The treatment of the vaginitis depends to a large extent on the organisms present and on their sensitivity to chemotherapeutic and antibiotic agents. The appropriate agent should be administered systemically, and at the same time it is an advantage to administer oestrone, 0.3 mg. twice daily by mouth, for three to four weeks. This latter increases the resistance of the vagina, but can have undesirable temporary side-effects such as enlargement of the breasts and uterine bleeding.

Intravaginal therapy is best avoided because of possible psychological reactions. However, under certain circumstances—trichomonal vaginitis, for example—it may be necessary to administer appropriate antiseptics by means of a small-sized vaginal pessary. Thrice-weekly instillations of a 0.5% aqueous solution of mercurochrome by means of a funnel and fine soft rubber catheter are useful in some cases.

Many other considerations arise, and these include measures to reduce the risk of transfer of the infection to other children, and the general management of the child and its mother to avoid introspective tendencies and over-anxiety.

Congenital Deformities of Fingers and Toes

Q.—*What can be done surgically to correct congenital absence or fusion of the fingers or toes? When is the best time to start treatment?*

A.—Little surgically can be done to correct congenital absence of fingers and toes. Later in life, provided some thumb metacarpal function remains, it may be possible to construct a gripping mechanism, but this will always depend upon the individual case.

Fusion of the fingers or toes is much more amenable to surgical treatment, and the excellence of the result depends upon the degree of webbing of the fingers. Where a simple skin web exists it can, under the best circumstances, be effectively separated to produce a good result without

deformity of the fingers. Where there is insufficient skin to make flaps to cover the fingers, a free graft may be introduced. Where the bones are fused the matter is much more difficult: although the fingers can be separated, mobile interphalangeal joints are not often obtained. The real difficulty lies in constructing an interdigital web which does not recur. The treatment of this condition is normally carried out by plastic surgeons. The best time to operate is between 3 and 5 years, when the child is fairly co-operative.

Aspirin Intoxication

Q.—*What adverse effects are known to result from prolonged daily use of aspirin and allied preparations? Is the drug habit-forming?*

A.—There is considerable individual variation in tolerance to the salicylates; but sweating, thirst, headache, dizziness, tinnitus, and nausea are signs of mild intoxication with these drugs. A more severe degree of intoxication is shown by fever, vomiting, diarrhoea, hyperpnoea, and severe excitation which may later change to coma. Aspirin has a particularly irritating effect on the gastric mucosa; in susceptible subjects it may produce gastric erosion with haematemesis if given as relatively insoluble tablets on an empty stomach. A few cases have been reported in which red striations of the skin, similar to those seen in Cushing's syndrome, have developed after very prolonged treatment.

Intolerance to the salicylates occurs occasionally and is shown by the development of a macular rash associated in the more severe cases with pyrexia and gastro-intestinal disturbance. The salicylates are not drugs of addiction.

Total Hysterectomy after the Menopause

Q.—*It was recently stated that even at an advanced age the ovaries are seldom inert. In view of this, what physical and psychological symptoms would be likely to follow total hysterectomy in a woman aged 60?*

A.—Although there is a good deal of evidence to suggest that the climacteric often occurs a few years after the menopause, and that meanwhile the ovaries are to some extent functional, few authorities would confidently assert that the ovaries produce significant amounts of oestrogen for very long after the menopause. Indeed, when oestrogen is found in circulation after the menopause it is often suggested that it has its origin in some other organ such as the adrenal cortex.

If a woman 60 years of age had the menopause at the usual time, and especially if it was accompanied by menopausal (or more strictly climacteric) symptoms, and if she shows the usual atrophic changes in the vagina and vulva, total hysterectomy with removal of both ovaries should not have any physical effects other than those directly related to the operation, nor is it likely to result in any psychological disturbance.

Wedding-ring Sensitivity

Q.—*A young woman is unable to wear her 9 carat gold wedding-ring because it causes an itchy rash to appear under it. What is the cause, and what treatment is advised?*

A.—Although occasionally psychological factors seem to be responsible for a localized eruption in this site, it seems more probable that in the case quoted the patient has become sensitized to the metal of her wedding-ring. Sensitivity to jewellery made of gold is not very common, but undoubtedly does occur. Such sensitivity usually lasts indefinitely, and the only solution is for the patient to avoid contact with the particular metal. In the case quoted, sensitivity may well be not to gold itself but to one of the metals used in the alloy. If this is so, different varieties of gold articles may not elicit the reaction. It might therefore be worth this patient trying a different gold ring to see its effect. Alternatively she will probably be able to wear a platinum ring without trouble.

NOTES AND COMMENTS

Syringes in General Practice.—Dr. DONALD MCGREGOR (Sutherland) writes: With regard to the question on this subject ("Any Questions?" July 25, p. 235) I would like to make the following comment. If syringes are carried in spirit, the needles must either be rinsed in boiled water in the patient's house before use (a tiresome procedure where water has to be carried and there is only a peat fire) or the patient must be submitted to the irritation of 95% alcohol subcutaneously. This can be guaranteed to lose patients. I suggest that the proper routine is to carry the syringes in spirit-proof cases without the spirit in them. The cases are sterilized in boiling water at the same time as their contents, and simply and quickly drained of water. Pasteur's experiments with retorts and turned-up mouths suggest that the syringes would, once housed in an empty, sterile, spirit-proof case, stay sterile indefinitely. Personally I resterilize any syringes I have not used each month to be on the safe side.

OUR EXPERT writes: Most of the spirit in the needle and in the barrel of a syringe which has been carried in a case containing 75% spirit can be removed by withdrawing the plunger several times and squirting. The last of the spirit can be removed by drawing up through the needle some sterile pyrogen-free water, or normal saline, carried in a rubber-capped bottle. Some of the solution that is to be injected may be used for this purpose if the makers of ampoules provide enough, as they often do, or if the injection is supplied in a rubber-capped bottle. If the syringe is to be used once only it can safely be carried, as your correspondent suggests, in an airtight case without spirit. But if the case contains six needles, and the barrel of the syringe is to be handled and used again with a different needle, it is safer to keep the syringe in 75% spirit.

Height and Weight Tables.—Mr. W. F. F. KEMSLEY (London, W.1) writes: On looking through the *Journal* of July 25 (p. 236) I have noticed in "Any Questions?" a reference to height and weight tables. In the reply it is stated that there are no up-to-date tables for heights and weights of British adults. This is not the case. Some time ago I compiled tables based on measurements made in 1943 on 27,000 men and 33,000 women. These tables will be found in the *Annals of Eugenics*, vol. 16, pp. 316–334, 1952, the paper being entitled "Body Weight at Different Ages and Heights." The paper explains how the tables were derived and gives comparisons between these new tables and earlier tables.

Dr. G. I. M. SWYER (London, W.C.1) writes: In the answer to the question on height and weight tables I am surprised to read: "Unfortunately, there are no up-to-date tables for the heights and weights of British . . . children." There is an excellent book by A. Sutcliffe and J. W. Canham, *The Heights and Weights of Boys and Girls*, John Murray, London, 1950. This book includes data on some 17,000 English boys and girls, very carefully selected from all parts of the country and from different school groups, so as to avoid any possible bias. The tables give figures for 5 to 17 years inclusive, and I think would certainly supply your questioner's requirements so far as children are concerned. Perhaps the most valuable feature of this book is the inclusion of tables of height and weight indices calculated in an analogous fashion to intelligence quotients. These enable one to decide, when either height or weight is considerably different from the average, whether the two are proportionate or not. Moreover, they enable one, when following the growth of a child, to decide whether the increments are occurring at the expected rate. I find this book to be quite invaluable in my dealings with growing children.

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